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The Cold Pressor Test in Pregnancy

BY

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IN 1933 Hines and Brown[1] described a standard test for measuring the variability of blood-pressure and discussed its significance as an index of the pre-hypertensive state. The test was based on two concepts regarding the aetiology of hypertension: first, that there is in its causation a constitutional factor which may be a hypersensitive vaso-motor centre or an abnormal reactor mechanism and, secondly, that there is also an environmental factor such as toxic or infective agents. It should theoretically be possible to recognize the constitutional factor in the individual years before the origin of clinical hypertension. The test as described by them is as follows: the subject is placed in a recumbent position for 15 minutes, or until the blood-pressure has reached the basal level; with the cuff placed on one arm, the opposite hand is placed in ice water at 4° to 5°C. The blood-pressure is taken at the end of 30 seconds and again at the end of 60 seconds. The hand is then removed from the bath and readings are taken every 2 minutes till the blood-pressure returns to its previous base level. The highest reading is recorded as a measure of the response. Normally the pressure returns to normal in 2 minutes after the hand is removed from the ice water. Hines and Brown consider that the response has a neurogenic reflex basis as it occurs too rapidly to be due to hormonal or chemical factors and still occurred after bilateral suprarenal-

ectomy in dogs. In appraising the value of the test three records are considered to be of importance: (*a*) the range of response, (*b*) the peak or ceiling, i.e. the highest blood-pressure recorded after the hand is placed in ice water, and (*c*) the time taken to return to normal after its removal from it. The range, i.e. the difference between the base level and the highest level recorded after the hand is placed in the bath, that may be considered normal, is of course somewhat arbitrary, and varies with different observers. Hines and Brown in their first paper placed it tentatively at 15 mm. Hg. and 2 years later in their second paper[2] at 22 mm. Hg. Randall[3] and his co-workers adopted 20 mm. as the normal limit, while Dieckmann[4] places it at 30 mm. Hg. The normal peak is usually placed at 145 mm. Hg. and, as previously stated, all observers agree that the time for return to normal after removal of the hand from the bath should not be more than 2 minutes.

As their tests were carried out on patients who were not pregnant Hines and Brown could not, of course, offer any conclusive proof that hyper-reactors would later develop permanent hypertension. That could only be shown by following up the patients tested for a number of years.

In pregnancy the development of the hypertension which ordinarily takes many years is hastened and it is, therefore, reasonable to suppose that by means of the test it would be possible early in pregnancy to pick out those patients who are destined to develop the hypertensive type of pre-eclamptic toxaemia.

Randall, Murray and Mussey were apparently the first to use the test in pregnant women, but the value of their observations is difficult to assess as all their patients had not been delivered when their paper was written. Dieckmann, Michel and Woodruff used the test on 152 normally pregnant women. Regarding an increase in range of 30 mm. Hg. or more as abnormal, they found that 90 patients were hyper-reactors, and of these 31.1 per cent developed toxaemia, while of 62 patients who gave a normal test 3 per cent developed toxaemia.

In the following series the tests were all carried out by the author personally so that a maximum of uniformity in the observations can be guaranteed. The technique was as described in the paper by Hines and Brown except that the blood-pressure readings were made on the arm that was placed in the ice bath, and that the hand remained in the bath for 2 minutes instead of one. The patient was rested in the recumbent position for 15 to

20 minutes or even longer, during which blood-pressure estimations were made at intervals of 5 minutes until it was judged that a basal reading had been obtained. The hand was then placed in the bath for 2 minutes, and during that time as many estimations as possible were made of systolic pressure. After removal of the hand from the bath the blood-pressure was recorded every 2 minutes until it returned to normal.

The observations were made on 75 primigrandae, all apparently normal. One patient subsequently aborted at 20 weeks. Two others fainted during the test, one before and the other just after putting the hand in the bath, so that further examination had to be abandoned. In addition, on the outbreak of war, some of the women were evacuated from London and were thus lost sight of. There were left 52 women upon whom the value of the test could be appraised. The details are given in the table and the results are briefly analysed below.

In 1933[5] the writer drew attention to the "early warning rise" of blood-pressure, so often present at the first antenatal examination and followed by normal blood-pressure readings at the next two or three examinations, and at subsequent ones by pre-eclamptic toxaemia of the hypertensive types which persisted usually till the end of pregnancy. This has also been studied in the present series and its value assessed alongside the three factors mentioned above.

In the analysis which follows the blood-pressure is considered raised if the systolic reading is 130 mm. Hg. or over and at the same time the systolic pressure is at least 70 mm. Hg.

Peak or ceiling. Of the 52 patients there were 23 in whom the highest peak of systolic pressure was 130 mm. Hg. or over; 12 of these developed pre-eclamptic toxaemia, i.e. 52 per cent. These 23 included 9 in whom the peak was 140 mm. Hg. or over, and 6 of these (67 per cent) developed toxaemia; in 5 of these the peak was 150 mm. Hg. or over and of them 4 (80 per cent) developed toxaemia. There were 29 patients in whom the peak of systolic pressure was below 130/70 mm. Hg., and of these 11 developed toxaemia (38 per cent). One of them was especially noteworthy. The peak was only 118 and yet the blood-pressure was raised at each subsequent antenatal examination, the highest recorded being 170/70 mm. Hg. It seems, therefore, that the higher the peak the more likely the patient is to develop toxaemia, and that when it reaches 150 mm. Hg. or over the chances of toxaemia arising are very great indeed. It must, however, be noted that in one case the peak was 152 mm. Hg. and yet the

patient remained apparently well until the end of pregnancy; and that, on the other hand, the absence of a high peak at the ice test does not preclude the possibility of the development of toxaemia later.

Range. The normal range is taken here as 20 mm. Hg., and any figure above that is regarded as excessive. The mean range of the patients who remained normal was 16.6, while of those who became toxaemic it was 14.1. In 9 patients the range was over 20 and 4 of these developed toxaemia (44.4 per cent). One patient had a range of 42 and yet remained well. This is the patient referred to above, who had a peak of 152 mm. Hg. There were 43 patients with a range of 20 or less, and of these 19 developed toxaemia (44.2 per cent). A study of the table will show that it was not unusual for patients with very low ranges to develop toxaemia. Our figures fail to support the view that a high range of systolic pressure is an indication of impending toxaemia.

Basal blood-pressure. As the range partly determines the peak and as we have seen that a high peak is a fairly good indication of impending toxaemia, it follows that a high basal blood-pressure, even though the range is normal, may be of importance as an indication that toxaemia will develop later. The mean basal pressure among the patients who remained normal was 108 mm. Hg., standard deviation 1.8 mm. Hg. Of those that developed toxaemia later it was 116 mm. Hg., standard deviation 10.6 mm. Hg. As the difference, viz. 8 mm. Hg., is more than twice the standard error of 2.8 mm. Hg. it is statistically significant.

Time taken to return to normal. Any time over 2 minutes was taken as excessive. The mean time of those that remained normal was 1.92 minutes, standard deviation 1.08 mm. Hg., while the mean time of those who became toxaemic was 2.08 minutes, standard deviation 1.33 mm. Hg. As the standard error is 0.35 mm. Hg. the difference between the two means (0.16) is not statistically significant. The time taken to return to normal was determined in 49 cases and in 13 of these the time was over 2 minutes. Of these 6 developed toxaemia (46 per cent). In one of the 7 that remained well the time was over 5 minutes, in another over 4, and in another $3\frac{1}{2}$. In 36 patients the time taken to return to normal was 2 minutes or less, and of these 16 developed toxaemia (44 per cent). It does not seem, therefore, that this observation is of any value in picking out the patients who will later develop toxaemia.

Early rise of blood-pressure. Of the 23 cases of toxaemia in the series an early rise of blood-pressure was observed in 9 (39 per cent). On the other hand, in every case but one in which an early rise was observed toxaemia occurred subsequently, i.e. it was observed in 10, and 9 of these (90 per cent) developed toxaemia later. It therefore appears that if an early rise occurs toxaemia will usually follow, but toxaemia may occur even if an early rise has not been observed.

Summary.

1. The paper records the results of the cold pressor test in a series of 52 normal primigrandae. The tests were undertaken in order to assess their value in picking out patients who might later develop pre-eclamptic toxaemia.

2. The peak of systolic pressure reached during the test seems to be of value in this respect. If the peak is over 150 mm. Hg. the patient is very likely, though not certain, to develop toxaemia later.

3. A high range, i.e. the difference between the basal level and the peak did not seem to be of any value. The same applies to the time taken to return to the normal basal level.

4. A high basal blood-pressure seems to be of value as an indication that toxaemia will develop later.

5. An early rise of blood-pressure, i.e. a systolic rise of 130 mm. Hg. or over at the first pre-natal examination, is a useful and easily observed indication of an instability of blood-pressure or perhaps of a high basic level that is often a forerunner of pre-eclamptic toxaemia. In the present series it was as useful an indication as a high peak.

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TABLE GIVING DETAILS OF CASES.

NOTE.—*Blood-pressure* is recorded in mm. Hg. (systolic only given).
Base level = difference between peak and range.

Number of patients	Range mm. of Hg.	Peak systolic blood-pressure	Base level	Time till normal in minutes	Early rise of blood-pressure	Toxaemia	
						Yes	No
752	30	140	110	3½	No		No
710	42	152	110	5+	No		No
693	15	135	120	1½	No	Yes	
611	14	112	98	½	No		No
451	30	142	112	2	Yes	Yes	
537	15	130	115	1½	No		No
718	10	140	130	1	Yes	Yes	
645	5	120	115	½	Yes	Yes	
270	10	130	120	2	Yes	Yes	
486	10	122	112	1	No		No
654	13	125	112	1¼	No	Yes	
758	12	122	110	1½	No		No
673	28	110	82	4+	No	Yes	
681	18	130	112	1½	Yes		No
813	15	122	107	1½	No		No
536	17	125	108	1½	No	Yes	
607	14	132	118	1½	No		No
484	18	132	114	3	No	Yes	
329	10	125	115	1¼	No		No
511	6	118	112	1	No		No
598	25	130	105	?	No		No
821	10	130	120	1½	No	Yes	
650	28	160	132	2	Yes	Yes	
879	20	150	130	2	Yes	Yes	
887	12	118	106	1½	No	Yes	
812	20	114	94	1¾	No		No
296	12	110	98	2	No		No
116	20	140	120	2	No		No
61	10	120	110	?	No		No
651	25	130	105	1½	No		No
820	3	118	115	?	No	Yes	
614	5	120	115	1	No	Yes	
578	20	130	110	4+	No		No
619	17	125	108	1	No		No
460	20	150	130	5½	Yes	Yes	
347	10	130/50	120	2	No		No
583	10	130	120	1	No	Yes	
834	14	120	106	3¼	No		No
767	24	154	130	1½	Yes	Yes	
747	12	130	118	1½	No		No
249	10	120	110	2	No	Yes	
444	30	120	90	3	No		No
354	5	115	110	3	No	Yes	
382	10	120	110	1½	No		No
630	20	120	100	2½	No		No
615	7	125	118	0	No	Yes	
450	2	130	128	0	No		No
18	20	110	90	2	No		No
150	15	130	115	5	Yes	Yes	
504	10	110	100	1	No		No
586	18	128	110	3	No		No
552	10	120	110	3	No	Yes	

External Hysterography

A Graphic Study of the Human Parturient Uterus and the Effect of Various Therapeutic Agents upon it.

BY

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Introduction.

Inefficiency of the expulsive forces, or uterine inertia, has been and still is commonly classified as (*a*) primary and (*b*) secondary, the former being a condition of inherent weakness of the uterine forces, the latter a condition of uterine exhaustion. The classification is not altogether satisfactory, and in recent years there has been a tendency to abandon it, for on the one hand pronounced primary inertia is rare, and on the other hand a weakening of the uterine contractions is frequently witnessed before the uterus can be said to be fatigued. All that need be said here is that uterine inertia is most commonly seen in the 1st stage of labour but may persist into or may first occur in the 2nd or 3rd stages. All degrees of severity are encountered, from those cases in which there is merely a harmless delay in cervical dilatation to those in which there is a complete cessation of uterine activity and labour is dangerously prolonged.

There can be no doubt that inefficiency of the expulsive forces is indirectly responsible for many of the disasters of midwifery. Delay, consequent upon poorness of the contractions, increases the incidence of interference to expedite delivery, which in turn, especially if unwisely applied, may be a cause of lacerations, haemorrhage and sepsis. Not only that, but many of the complications of labour become increasingly dangerous and difficult to manage in the presence of inefficient uterine contractions—occipito-posterior positions of the vertex fail to rotate, heads fail to mould in cases of disproportion, and ante-partum haemorrhage is less easily controlled.

Expression of the foetus is brought about by contractions of the uterus aided during the 2nd stage of labour by the auxiliary forces, and it is natural to expect that labour may be prolonged, sometimes by one, sometimes by the other and occasionally by both being at fault. Unfortunately, there is no absolute standard by which the forces may be gauged or compared. The amount of pain experienced by the patient is certainly no guide, for it is common knowledge that in some cases of uterine inertia feeble ineffective contractions may cause intolerable suffering; on the other hand contractions sufficiently powerful and effective to complete labour in a relatively short time may be present without causing the patient distress.

Clinically, the effectiveness of uterine contractions can be roughly gauged in two ways: by palpating the uterus during contractions and estimating their duration, frequency and strength; and secondly, by noting the effect of contractions upon dilatation of the cervix, always remembering, however, that factors other than the strength of the uterine contractions influence cervical dilatation. Such methods have obvious limitations and only serve to make more apparent the need for a satisfactory method of estimating the forces of labour.

It is, primarily, as a contribution to the latter problem that this paper has been written. A method of recording the forces of labour is described and a preliminary report of the observations made by this method presented in the form of a systematic graphic study of the human parturient uterus and the effect of various therapeutic agents upon it.

External Hysterography.

Literature.

Many endeavours have been made to measure the forces of labour. Mathews Duncan[1] (1868) appears to have been the first to attempt such an estimation, his method being to ascertain the force required to rupture the foetal membranes by water-pressure. He also estimated by means of a dynamometer attached to the forceps the amount of force required to extract the child.

Other workers repeated his experiments, but it remained for Schatz[2] (1872) to perfect a method of obtaining permanent graphic records of the uterine contractions. His tokodynamometer consisted of a small rubber bulb or *kolpeurynterblasé* (of 70 to 80 c.c. capacity) filled with water and connected in a closed system by means of a T-piece to a revolving recording

drum and mercury manometer. Under chloroform anaesthesia the bulb was introduced into the uterus, past the presenting part, taking care not to rupture the membranes. With this apparatus Schatz was able to obtain simultaneously the force in millimetres of mercury exerted by the uterine contractions and was able to demonstrate the salient features of uterine activity.

Poullet[3] (1878) in an attempt to determine the additional force exerted by the abdominal muscles constructed his tocograph, consisting essentially of two rubber bulbs, one introduced into the uterus, and one into the rectum, above the presenting part, each connected by tubing to a mercury manometer with float and a writing point recording on a kymograph. His results, however, were rather inconclusive.

Polaillon[4] (1879) modified Schatz's method by placing a small rubber balloon just within the cervix and connecting it to a recording tambour, but met with less success. Using similar apparatus, Acconci[5] (1891) made several observations regarding the action of various therapeutic agents on uterine contractions, and Doehnoff[6] (1892) demonstrated the depressant action of chloroform anaesthesia.

Westermark[7] (1893) objected to the methods of his predecessors on the grounds that to introduce a rubber bulb of 70 to 80 c.c. capacity into the uterus not only gave rise to the risks of intra-uterine manipulations but mechanically stimulated uterine contractions above the normal due to the bulk added to the uterine contents and subjected patients to otherwise unnecessary anaesthesia. He, therefore, used a very small bulb (of 2 c.c. capacity) attached to a urethral catheter and connected to a recording drum mechanism, and made many exhaustive observations of pressure-changes in the uterus during the various stages of labour.

The first worker to employ an external method of recording uterine contractions was Schaffer[8] (1896). He devised an instrument which was applied to the abdomen overlying the distended uterus by means of straps and estimated the force exerted by the contracting uterus as being equal to as much as 220 mm. of mercury.

Ruebsamen[9] (1920) published a method called "external hysterography" which was a departure from all the procedures of his predecessors. The apparatus consisted of a device of known weight suspended from a frame by means of cord and pulleys so as to rest on the abdomen covering the uterus, and connected to a recording drum. It is obvious that displace-

ment of the weight was caused not only by contraction of the uterus but by any movement of the patient, coughing or sneezing, and movement of the bed. Most of Ruebsamen's observations concerning the action of pituitary extract, ergot and quinine were conducted after delivery, but the unsuitability of such an apparatus for experiments in the 1st and 2nd stages of labour is at once apparent.

More recently Bourne and Burn[10] (1927) have contributed a good deal to the graphic study of uterine activity. Their work dealt chiefly with the action and dosage of pituitary extract and ergot alkaloids on the uterus in labour. The method they employed was that of a small intra-uterine bag connected by water-filled tubing to a mercury manometer tracing on a slowly revolving drum.

Rucker[11] (1930), too, has studied the effect of various anaesthetics and analgesics, pituitary extract, thymophysin and ergot on the contractions of the uterus, his method being to insert a Voorhees's bag into the cervix and connect it to a mercury manometer carrying a writing point inscribing on a smoked drum.

One of the most valuable contributions to the subject in recent years is that of Dodek[12] (1932). He described a new method of "external hysterography" and published an admirable report showing graphically the effect of certain anaesthetics, sedatives and oxytocics on the uterus in labour. The apparatus which he used consisted of a plunger affecting the diaphragm of a pneumatic chamber which was connected in turn in a closed-air system to a tambour writing on a recording drum. The plunger and pneumatic chamber were held in a tripod-like structure and applied to the patient's abdomen so that increase in the antero-posterior diameters of the uterus and maternal abdomen occurring with each contraction caused an upward movement of the plunger and corresponding compression in the closed-air system affecting the writing point of the tambour.

The works of Chassar Moir[13] on the identification and action of the ergot alkaloids, the action of oxytocics in the post-partum period and other problems concerning uterine activity are well known. In repeated experiments he used two methods of recording uterine contractions. One was an adaptation of the method of Bourne and Burn. A small bag, containing when fully distended 12 c.c. water, was mounted on a thin rubber tube, strengthened by an internal stylette. The whole was steri-

lized by boiling and with full aseptic and antiseptic precautions was carefully inserted into the uterine cavity. The bag was connected by water-filled tubing to a mercury manometer tracing on a slowly revolving drum. The second apparatus was designed to record changes in the shape of the uterus occurring during uterine contractions and was a simplified form of the apparatus used by Dodek. It consisted of a levered hammer impinging on the diaphragm of a water-filled chamber, the whole supported in a tripod-like structure applied to the abdomen and connected in a closed-water system to a recording tambour and revolving drum. Contraction of the uterus caused an upward movement of the hammer which was transmitted by water-pressure to the writing tambour.

Method of Study.

Briefly, there are two ways in which the activity of the parturient human uterus has been and may be recorded.

1. By the introduction of a metreurynter into the uterus which will record changes in intra-uterine pressure: internal hysterography.

2. By applying an apparatus to the maternal abdomen which will respond to changes in the shape of the uterus occurring during contractions: external hysterography.

The hysterographic study which follows was planned to be a comprehensive report on the behaviour of the human uterus in labour under the influence of various therapeutic agents. With this in mind it was realized that any method of recording chosen should be simple, easily applicable in all cases and not distressing to the patient; and from this viewpoint the advantages of external hysterography were at once apparent.

It was appreciated that the internal method, involving as it does the introduction of a hydrostatic bag into the uterus, would subject each patient to an otherwise unnecessary anaesthetic, which itself might influence the uterine contractions. With the introduction of a foreign body into the uterus there would be the consequent risk of infection—however small this risk may be in a well-conducted maternity department. More important still, the presence of the metreurynter in the uterine cavity might itself stimulate the uterine contractions, increasing their force and frequency and so giving an unfair estimation of the uninfluenced uterine activity. Lastly, internal hysterography involves a quite elaborate technique—pre-operative preparation

of the patient and intra-uterine part of the apparatus, anaesthesia and the frequent services of assistants—and it was felt that valuable opportunities for study would be lost, especially in the later stages of labour, if this method was adopted.

On the other hand, the expected disadvantages of external hysterography would be that direct readings of the intra-uterine pressure could not be obtained—of little import in a comparative study such as that planned; the recording might be a little erratic and to some extent influenced by such factors as stoutness of the abdominal wall; and the difficulty of eliminating extraneous movements—the abdominal respiratory movements, pulsations transmitted from the aorta and movements of the patient.

The apparatus employed in this study is a modification of that of Dodek and is similar to that used on occasions by Chassar Moir. It is illustrated in Figs. 1 and 2. It consists essentially of a levered cork hammer impinging on the rubber diaphragm of a pneumatic chamber which is connected in turn in a closed-air system to a sensitive tambour writing on a recording drum. The pneumatic chamber and levered hammer are held in a four-legged support with a circular base which is applied to the maternal abdomen overlying the distended uterus.

Advantage is taken of the principle that during each uterine contraction the antero-posterior diameters of the uterus and maternal abdomen increase. This causes an upward deflection of the hammer which produces, *via* the diaphragm, corresponding compression of the air column which is transmitted to the tambour and recording mechanism. The abdominal part of the apparatus is constructed of light metal and is applied to the abdomen over the point of maximal contraction, which is usually in the immediate neighbourhood of the umbilicus, by two strips of elastoplast strapping as illustrated. By means of a thumb-screw the pneumatic chamber is lowered in its support so that the hammer rests on the abdomen and makes contact with the diaphragm. The outlet tube of the pneumatic chamber is then connected by rubber tubing to the tambour. This tambour is fitted with a light ink pen and traces on an electric recording drum of 12 inches diameter rotating once every 3 hours. A time marker with light ink pen is incorporated with the recording drum and marks one-minute intervals.

The apparatus described has been used to the exclusion of any other in collecting the material presented in this report

and has proved itself eminently satisfactory. It is light in weight, is not annoying to the patient and is readily applied to the abdomen at any stage of labour without interfering with labour's progress or retarding preparations for delivery. Applied in the manner described it rides upon the abdomen and is uninfluenced by the normal abdominal respiratory movements or pulsations transmitted from the aorta; the patient, too, is permitted a fairly wide range of movement without affecting the recording tambour. Violent contractions of the abdominal muscles, such as occur during coughing, vomiting or bearing down efforts, cause additional compression in the air system which is seen in superimposed lines on the tracing and readily recognized. Foetal movements, too, if they occur directly under the apparatus, produce transitory superimposed lines on the tracings.

By the method of external hysterography described many individual studies of uterine activity have been completed. Tracings have been made during the 1st and 2nd stages of labour in varying circumstances and the clearest examples in each class photographed for reproduction in this report. It should be clearly understood that there has been no selection of cases for study—the method employed is applicable to and capable of yielding satisfactory tracings in all cases. Certain circumstances have prevented study in every case, e.g. patients delivered immediately after admission, several patients in labour simultaneously, and patients in whom some obstetrical complication has fully occupied the time of the investigator—but with such exceptions the tracings forming the basis of this report have been obtained in consecutive cases.

The scheme of study adopted is:

(i) The Uninfluenced Uterus: the presentation of tracings illustrating the characteristic features of normal and inert labours.

(ii) The Influenced Uterus: the presentation of tracings illustrating the effect of various agents, commonly employed therapeutically in normal and inert labours.

The agents studied are classified as follows:

1. *Anaesthetics.*
   Gas and oxygen.
   Ether.
   Chloroform.

2. *Analgesics and Sedatives.*
   Potassium bromide and chloral hydrate.
   Morphia.
   Morphia and hyoscine.

3. *Oxytocics.*
   Quinine.
   Pituitrin.
   Pitocin.
   Thymophysin.
   Oestrin.
   Acetylcholine.

So far as possible tracings are presented in the case of each agent illustrating its action on:

(*a*) normal 1st stage contractions,

(*b*) inert 1st stage contractions,

(*c*) normal 2nd stage contractions,

(*d*) inert 2nd stage contractions.

The terms inert and inertia are used in this study as implying inefficiency of the uterine forces occurring at any stage of labour and of any severity. The designation of any tracing as inert means only that the expulsive forces were inefficient at the time of study and in many such instances the inertia was a temporary complication and the labour not unduly prolonged.

The Uninfluenced Uterus.

When the 1st stage of labour is well established the uterine contractions recur at intervals of from 1 to 4 minutes and last usually about 1 minute. A contraction reaches its maximum slowly, is maintained at its acme for a very short time, and then undergoes gradual relaxation. Usually the contractions recur at regular intervals and are of approximately constant intensity and duration but not necessarily so, and occasionally contractions are double, i.e. before complete relaxation has occurred the uterus may be thrown into a second contraction which may be more intense than the first.

Fig. 3 is a reproduction of a tracing showing the normal 1st stage contractions. The patient was a multipara and the vertex presented in the left occipito-posterior position. The cervix at the time of study was two fingers dilated. The contractions, it

FIG. 1

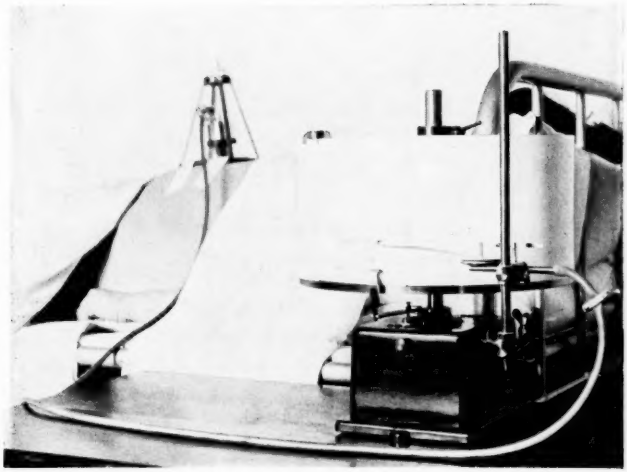
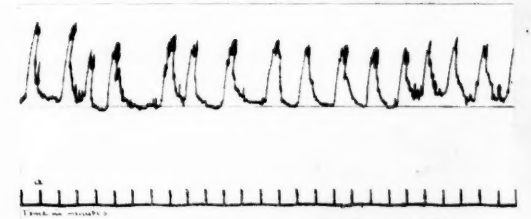


FIG. 2

Normal first stage contractions. Multipara. vertex. Left occipito-posterior. Two fingers dilatation. Contractions painful, patient comfortable between pains. Note (a) double contraction, (b) irregular intensity of contractions.

FIG. 3



Normal second stage contractions. Primipara. Vertex. Left occipito-anterior. Contractions painful, patient comfortable between pains. Noto (a) voluntary expulsive efforts or "bearing down".

FIG. 4

can be observed, recur at intervals of approximately 2 minutes, but there is a certain variation in the length of this interval as well as in the intensity and duration of the contractions. Point *a* in the tracing illustrates a typical double pain. The prolonged interval following this double pain is probably of the nature of a refractory period. At *b* the irregular intensity and duration of the contractions is well seen. Each contraction reaches its maximum slowly but not always gradually, and it is not unusual for a contraction to be maintained at a certain level for a short period and then suddenly increase in intensity. The acme is maintained a very short time before slow relaxation sets in. The contractions are not painful throughout their entire phase—for a short time after the commencement of each contraction there is no sensation of pain, and all pain disappears before the stage of complete relaxation has been reached. Points *x* and *y* in the tracing indicate the commencement and cessation of pain.

In the 2nd stage of labour the uterine contractions usually increase in intensity and frequency. The pains gradually become more expulsive or bearing down in character and the abdominal muscles are brought into play to help in the expulsive efforts. At first the abdominal muscles contract under the volition of the patient, but later their contractions become to a large extent involuntary.

A typical tracing of normal contractions in the 2nd stage is reproduced in Fig. 4. The patient was a primipara with a left occipito-anterior presentation. The contractions in this example recur at intervals of about 2 minutes, and it will be noticed that, compared with the smooth even curves seen in the 1st stage, each contraction after point *a* bears at its summit accessory lines superimposed on the basic curve due to the several expulsive efforts made by the patient. Owing to the slow speed at which the recording drum revolves, these accessory tracings lie very close together so that individual lines may be indistinguishable.

The transition from the 1st to the 2nd stage of labour can be clearly demonstrated by external hysterography. Fig. 5 represents this transition in a multipara with a right occipito-anterior presentation. After point *a* in the tracing each subsequent contraction reveals the accessory superimposed lines of the early 2nd stage. This figure, too, demonstrates the accessory tracings produced by vomiting, and at one point it will be observed how vomiting stimulated a premature contraction.

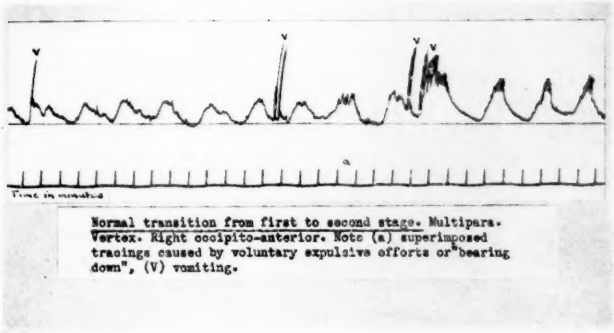
Normally this transition in the character of uterine activity commences with the completion of obliteration and dilatation of the cervix, but hysterographically it has been demonstrated on several occasions that it is not unusual for a patient to bear down before the cervix is fully dilated. Fig. 6 represents a tracing obtained in a primiparous patient in whom the vertex presented in the left occipito-anterior position. At the time of study the cervix was not quite fully dilated, there being considerable anterior lip and a little posterior lip remaining; yet the contractions at point *a* and certain succeeding contractions bear quite unmistakably the superimposed tracings of bearing down efforts.

Uterine inertia or inefficiency is a condition which may be seen at any stage of labour and be of any degree of severity. It has been observed clinically, on many occasions, that cases tend to conform to one of two types—in the first the contractions, while fairly normal in character, are of feeble intensity and duration, recur at infrequent intervals, and cause little discomfort. In the second the contractions are colicky and painful, of quite irregular intensity, duration and frequency, and are ineffective in bringing about the dilatation of the maternal passages and expulsion of the child.

Fig. 7 is a representation of inert contractions in the 1st stage in a primipara with a left occipito-anterior presentation. In this example the contractions, while recurring at quite frequent intervals, are poor and of irregular intensity and duration. The transitory impressions made by foetal movements are seen in this tracing. An example of an inert 2nd stage is shown in Fig. 8. The patient was a multipara with a vertex presentation in the left occipito-anterior position. At the time this tracing was obtained the 2nd stage of labour had been in progress 1 hour with satisfactory contractions and the presenting part was well down on the pelvic floor, but in spite of this it will be noticed that at point *a* the pains are going off.

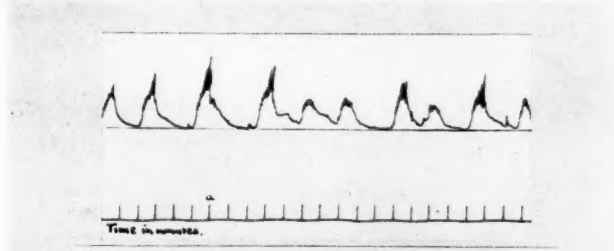
The Influenced Uterus. Anaesthetics:

Nitrous oxide gas. With a fuller realization of its valuable anaesthetic properties and improvements in the technique of administration the indications for the employment of nitrous oxide gas have been continually extended so that to-day it ranks as the inhalation anaesthetic of choice in the majority of surgical procedures. In obstetrics it is now used widely both as an analgesic and an anaesthetic, and it is, therefore, of some importance



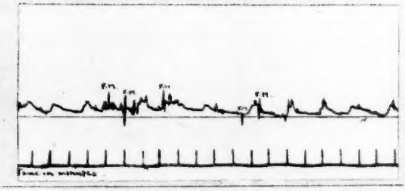
Normal transition from first to second stage. Multipara. Vertex. Right occipito-anterior. Note (a) superimposed tracings caused by voluntary expulsive efforts or "bearing down", (V) vomiting.

FIG. 5



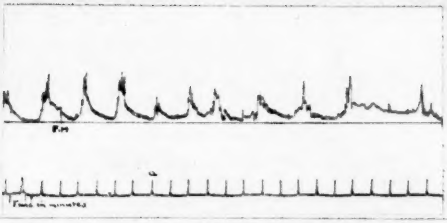
Normal first stage contractions.(Late). Primipara. Vertex. Left occipito-anterior. Almost full dilatation. Contractions painful. Note (a) superimposed tracings caused by voluntary expulsive efforts or "bearing down".

FIG. 6



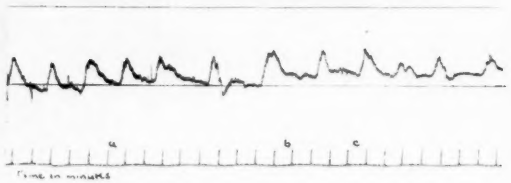
Inert first stage contractions. Primipara. Vertex. Left occipito-anterior. One finger dilatation. Poor contractions of irregular intensity and duration. Note (F.M.) foetal movements.

FIG. 7



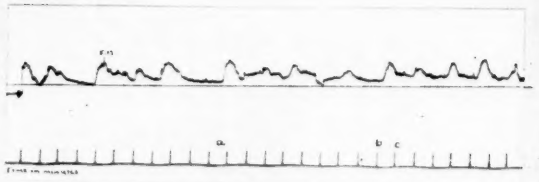
Inert second stage contractions. Multipara. Vertex. Left occipito-anterior. Poor contractions of irregular intensity and duration. Note (a)"pains going off", (F.M.) foetal movements.

FIG. 8



Gas and air analgesia - Normal first stage. Primipara. Breech. Left sacro-anterior. Three quarters dilatation. Note (a) Gas and air analgesia, (b) increased tonicity, (c) no effect on progress of labour but patient more comfortable.

FIG. 9



Gas and air analgesia - Inert first stage. Primipara. Vertex. Right occipito-posterior. Three fingers dilatation. Note (a) gas and air analgesia, (b) no effect on progress of labour but patient more comfortable during pains, (c) increased tonicity, (F.M.) foetal movements.

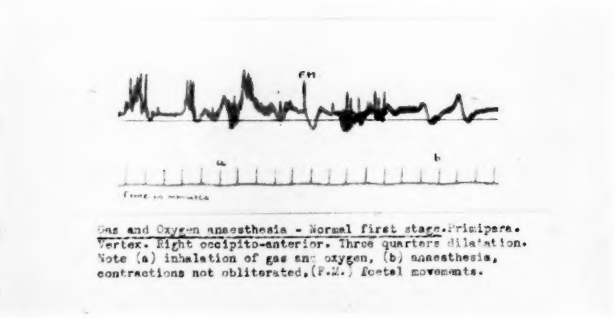
FIG. 10

Gas and air analgesia - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) gas and air analgesia, (b) no effect on progress of labour but patient more comfortable during pains, (c) increased tonicity, (F.M.) foetal movements.

FIG. 11

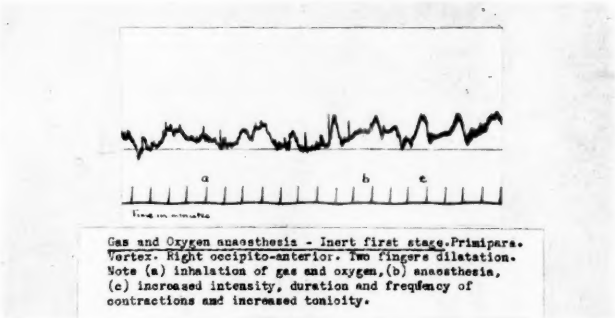
Gas and Air analgesia - Inert second stage. Primipara. Vertex. Left occipito-anterior. Note (a) inhalation of gas and air, (b) no effect on progress of labour but patient more comfortable during pains, (c) increased tonicity.

FIG. 12



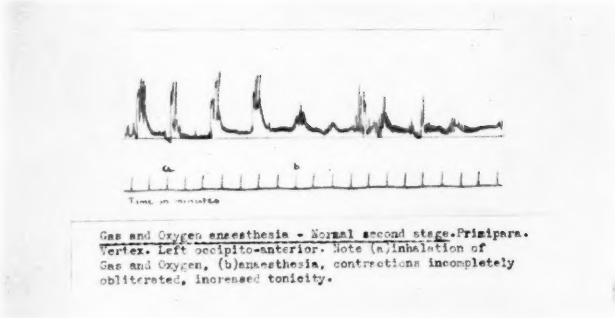
Gas and Oxygen anaesthesia - Normal first stage.Primipara. Vertex. Right occipito-anterior. Three quarters dilatation. Note (a) inhalation of gas and oxygen, (b) anaesthesia, contractions not obliterated.(F.M.) foetal movements.

FIG. 13



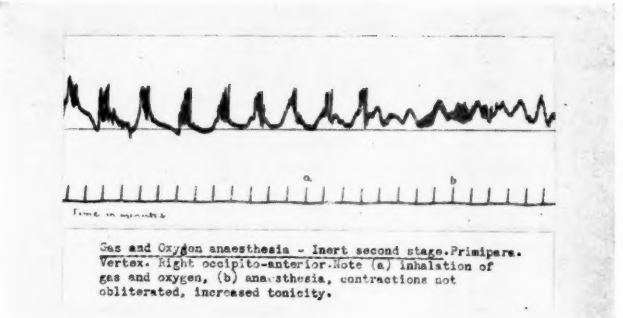
Gas and Oxygen anaesthesia - Inert first stage.Primipara. Vertex. Right occipito-anterior. Two fingers dilatation. Note (a) inhalation of gas and oxygen,(b) anaesthesia, (c) increased intensity, duration and freqfency of contractions and increased tonicity.

FIG. 14



Gas and Oxygen anaesthesia - Normal second stage.Primipara. Vertex. Left occipito-anterior. Note (a)Inhalation of Gas and Oxygen, (b)anaesthesia, contractions incompletely obliterated, increased tonicity.

FIG. 15



Gas and Oxygen anaesthesia - Inert second stage.Primipara. Vertex. Right occipito-anterior.Note (a) inhalation of gas and oxygen, (b) anaesthesia, contractions not obliterated, increased tonicity.

FIG. 16

to be able to demonstrate graphically its effect on uterine activity.

Administered as an analgesic, nitrous oxide gas does not appear to have any depressant effect on the contracting uterus; indeed it would seem on occasion that this gas may even stimulate or increase uterine contractions. Figs. 9 and 10 show the effect of gas and air analgesia in the 1st stage of labour. At point *a* in Fig. 9 the inhalation of gas and air during each contraction was commenced, Minnitt's apparatus being used for the purpose. The uterine contractions are seen to continue without depression and at *b* there is a tendency to an increase in their intensity and a quite definite increase in the tonicity of the uterus as demonstrated by a rise of the base line of the tracing. Fig. 10, also, shows an increase in the tonicity of the uterus. The effect of gas and air in the 2nd stage is similar and is represented in Figs. 11 and 12. In each case there is an increase in the uterine tonicity, and it would appear that this is a constant accompaniment of gas and air analgesia. Gas and air, then, constitutes a very valuable analgesic in obstetrics. It comforts the patient and enables her to bear her pains with greater fortitude without in any way interfering with the progress of labour.

Even when administered in sufficient concentration to produce anaesthesia, nitrous oxide gas has little or no depressant action on the contracting uterus, and again an increase in the tonicity of the uterus appears to be a constant feature. Figs. 13, 14, 15 and 16 are reproductions of tracings illustrating uterine activity under the influence of gas and oxygen anaesthesia. Fig. 13 represents a late 1st stage with evident bearing down efforts. Inhalation of gas and oxygen was commenced at *a* so that at *b* the patient was anaesthetized. The voluntary or semi-voluntary bearing down efforts, it will be noticed, are obliterated by anaesthesia but the uterine contractions continue without apparent depression.

That no increase in tonicity is seen in this tracing is accounted for by the fact that at the commencement of the recording the patient was already under the influence of gas and air analgesia. In Fig. 14—an inert 1st stage—the uterine contractions actually improve under anaesthesia and there is a well evidenced increase in uterine tonicity. The effect of gas and oxygen anaesthesia in the 2nd stage is to obliterate the voluntary or semi-voluntary bearing down efforts without unduly influencing the uterine contractions. Thus, in Fig. 15, although at point *b*

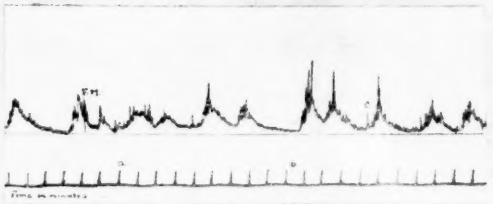
the degree of anaesthesia was quite deep, the contractions are still in evidence and uterine tone is increased. Fig. 16 shows the same features in a 2nd stage with rather poorer pains.

Ether. In this country pure ether is not very extensively employed in obstetric practice, its main disadvantage being that it tends to aggravate or induce bronchial catarrh. It is, however, quite often used to supplement the action of gas and oxygen and is also used in mixtures with chloroform.

Briefly its action would seem to be that, while it acts as an efficient analgesic and anaesthetic, it depresses the uterine activity in direct proportion to the depth to which it is administered. Thus, when it is given as an analgesic, *i.e.* in doses of approximately 1 drachm at the commencement of each contraction, the sensation of pain is largely removed, but the uterine contractions are unaffected and the progress of labour is not retarded. These points are borne out in Figs. 17, 18, 19 and 20, representing examples of the normal and inert 1st and 2nd stages, and require no further comment.

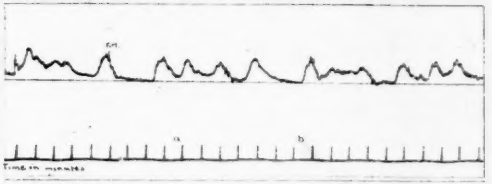
When given in sufficient concentration to produce unconsciousness, ether depresses the activity of the uterus. In direct proportion to the depth of anaesthesia are the intervals between contractions prolonged and the intensity of contractions decreased. In Fig. 21 drop ether was commenced at point *a* but the amount of ether given was small, and 10 minutes later although the patient was unconscious the depth of anaesthesia was not great. Thus it will be observed that at point *b* the uterine contractions are only incompletely obliterated. This figure, too, illustrates another feature which may be seen in the several tracings, depicting the influence of anaesthesia, and that is the increased thickness of the traced line due to the deeper abdominal respiratory movements of anaesthesia. Fig. 22 presents a rather similar picture in an inert 1st stage. The effect of ether anaesthesia in a normal 2nd stage is depicted in Fig. 23. Here the expulsive bearing down efforts are removed, and at point *b* anaesthesia is relatively deep and the uterine contractions largely obliterated. In the same way in Fig. 24 the uterine activity is diminished in proportion to the depth of anaesthesia.

Chloroform. In domiciliary obstetric practice, at least, chloroform continues to be the anaesthetic most favoured in this country. Conveniently administered, it is safe in ordinary simple deliveries and, given *à la reine*, it has been the standby of obstetricians for several generations.



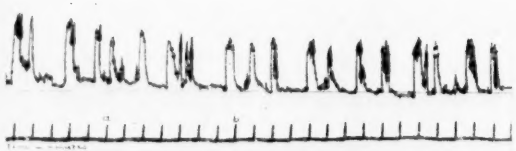
Ether analgesia - Normal first stage.Primipara. Vertex. Left occipito-anterior. Three quarters dilatation.Note (a) inhalation of ether dr. 1 approx. during each pain,(b) no effect on progress of labour but patient more comfortable during pains, (C)cough, (F.M.)footal movements.

FIG. 17



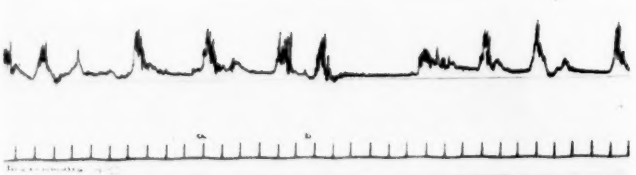
Ether analgesia - Inert first stage. Primipara. Vertex. Right occipito-posterior.Three fingers dilatation. Note (a) inhalation of ether dr. 1 approx. during each pain, (b) no effect on progress of labour but patient more comfortable during pains, (F.M.) footal movements.

FIG. 18



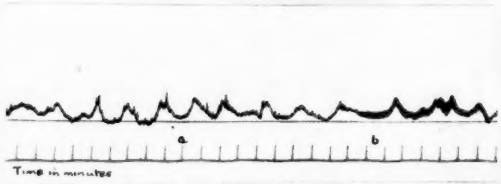
Ether analgesia - Normal second stage.Primipara. Vertex. Left occipito-anterior. Note (a) inhalation of ether dr. 1 approx. during each pain, (b) no effect on progress of labour but patient more comfortable during pains.

FIG. 19



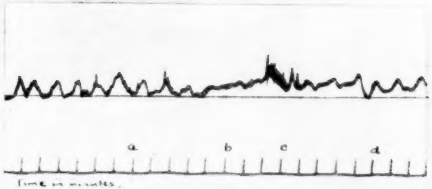
Ether analgesia - Inert second stage. Primipara. Vertex. Left occipito-anterior. Note (a) inhalation of ether dr. 1 approx. during each pain, (b) no effect on progress of labour but patient more comfortable during pains.

FIG. 20



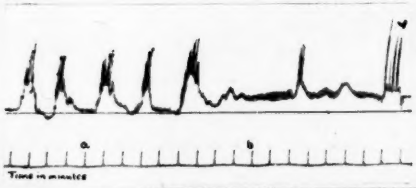
Ether anaesthesia - Normal first stage. Primipara. Vertex. Left occipito-posterior. Three fingers dilatation. Note (a)inhalation of ether, (b)anaesthesia, contractions incompletely obliterated.

FIG. 21



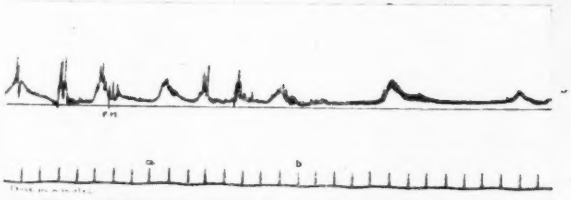
Ether anaesthesia - Inert first stage. Primipara.Vertex. Left occipito-posterior. Half dilatation. Note (a) inhalation of ether, (b) anaesthesia, contractions incompletely obliterated, (c)ether discontinued, (d) contractions recur.

FIG. 22



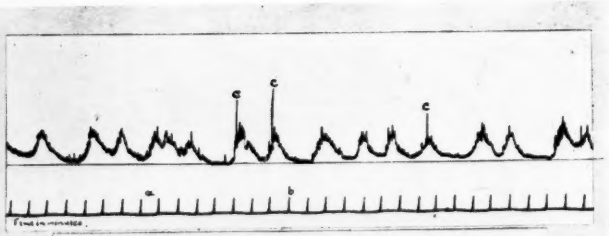
Ether anaesthesia - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) inhalation of ether, (b) anaesthesia, contractions obliterated, (V) vomiting.

FIG. 23



Ether anaesthesia - Inert second stage. Primipara. Vertex. Left occipito-anterior. Note (a) inhalation of ether, (b) anaesthesia, contractions obliterated, (F.M.) foetal movements.

FIG. 24

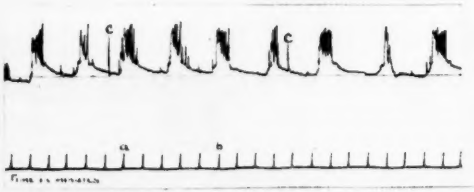


Chloroform analgesia - Normal first stage. Primipara. Vertex. Left occipito-anterior. Three quarters dilatation. Note (a) inhalation of chloroform m. 20 approx. during each pain, (b) no effect on progress of labour but patient more comfortable during pains.

FIG. 25

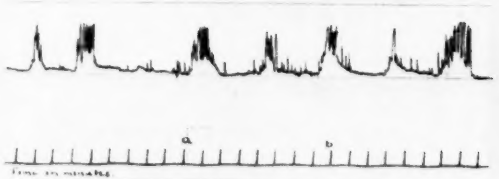
Chloroform analgesia - Inert first stage. Primipara, Vertex. Right occipito-posterior. Two fingers dilatation. Note (a) inhalation of chloroform m. 20 approx. during each pain, (b) no effect on progress of labour but patient more comfortable during pains, (F.M.) foetal movements.

FIG. 26



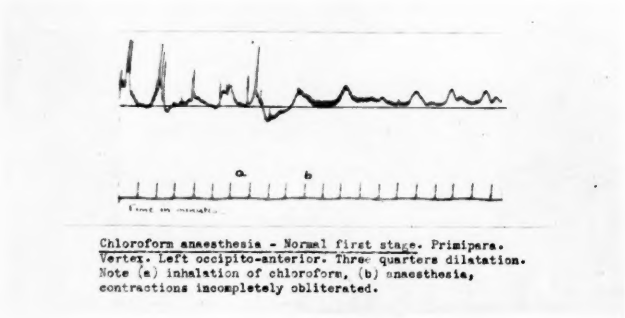
Chloroform analgesia - Normal second stage. Multipara. Vertex. Right occipito-anterior. Note (a) inhalation of chloroform m.20 approx. during each pain, (b) no effect on progress of labour but patient more comfortable during pains, (C) cough.

FIG. 27



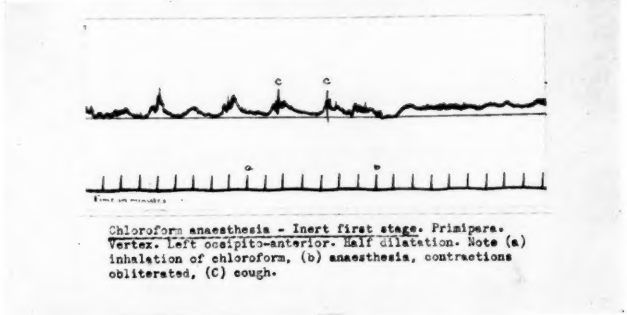
Chloroform analgesia - Inert second stage. Multipara. Vertex. Right occipito-anterior. Note (a) inhalation of chloroform m.20 approx. during each pain, (b) no effect on progress of labour but patient more comfortable during pains.

FIG. 28



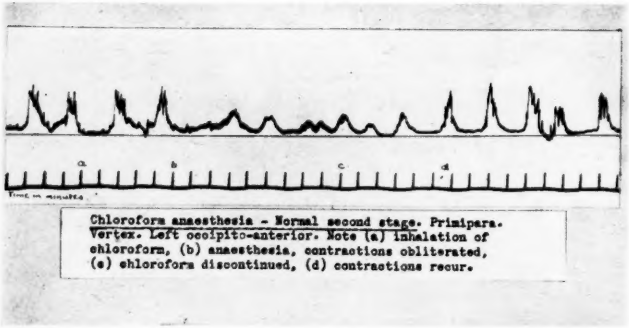
Chloroform anaesthesia - Normal first stage. Primipara. Vertex. Left occipito-anterior. Three quarters dilatation. Note (a) inhalation of chloroform, (b) anaesthesia, contractions incompletely obliterated.

FIG. 29



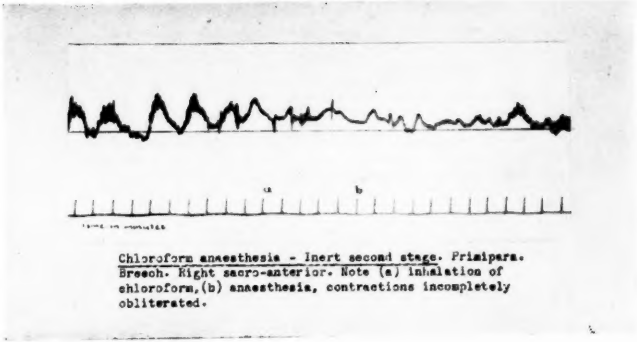
Chloroform anaesthesia - Inert first stage. Primipara. Vertex. Left occipito-anterior. Half dilatation. Note (a) inhalation of chloroform, (b) anaesthesia, contractions obliterated, (C) cough.

FIG. 30



Chloroform anaesthesia - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) inhalation of chloroform, (b) anaesthesia, contractions obliterated, (c) chloroform discontinued, (d) contractions recur.

FIG. 31



Chloroform anaesthesia - Inert second stage. Primipara. Breech. Right sacro-anterior. Note (a) inhalation of chloroform, (b) anaesthesia, contractions incompletely obliterated.

FIG. 32

Chloroform is a powerful analgesic and anaesthetic, and, like ether, it depresses the activity of the uterus in direct proportion to the depth to which it is administered. Fig. 25 reproduces a tracing of normal contractions of the 1st stage in a patient given chloroform analgesia. At point *a* in the tracing the administration of chloroform in doses of approximately 20 minims at the commencement of each contraction was instituted, chloroform capsules or brisettes being used for the purpose. The succeeding contractions do not reveal any depression either of intensity, duration or frequency. Fig. 26 shows a similar result to the giving of small amounts of chloroform in an inert 1st stage. In the 2nd stage of labour, chloroform analgesia produces precisely similar results, as seen in Figs. 27 and 28. That is to say, chloroform in small doses produces satisfactory analgesia without retarding the progress of labour.

When the concentration of chloroform is increased so as to produce anaesthesia the uterine contractions are decreased in intensity, duration and frequency, and can be obliterated altogether with deep anaesthesia. The inhalation of chloroform was commenced at point *a* in Fig. 29. The depth of anaesthesia was never great, and it will be observed that at *b* the contractions are by no means completely obliterated. In Fig. 30 an inert 1st stage is represented. Induction of anaesthesia was begun at *a* and from *b* onwards the contractions are almost completely obliterated. In the 2nd stage the effect of chloroform anaesthesia is, first, to abolish the voluntary bearing down efforts and then to diminish the uterine contractions in proportion to the depth of anaesthesia. Fig. 31 is interesting in that it reveals the manner in which one may control the contractions of the uterus with chloroform at will. The inhalation of chloroform was commenced at point *a*. At point *b* the superimposed tracings of the 2nd stage are no longer evident and the succeeding contractions are diminished in intensity and frequency. With the withdrawal of the anaesthetic the contractions begin to recur and increase in intensity and frequency at about the same rate at which they were decreased. The effect of chloroform anaesthesia during a more inert type of 2nd stage is seen in Fig. 32.

Analgesics and Sedatives.

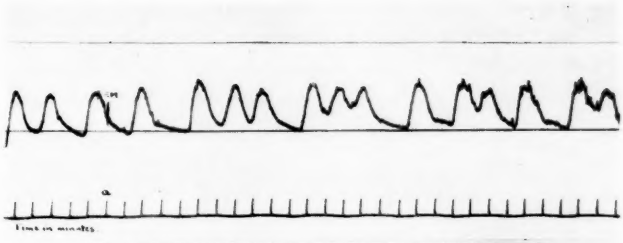
Potassium bromide and chloral hydrate. Clinically, potassium bromide and chloral hydrate would appear to have one of two effects in labour if any: on the one hand, it may give the patient

a period of sleep following which the labour proceeds with renewed vigour; on the other hand, it may have the quite definite effect of hastening labour, delivery following rapidly on its administration.

In repeated studies the investigator has been unable to demonstrate that potassium bromide and chloral hydrate has any very definite effect on the uterus in labour. Figs. 33 and 34 are two tracings from patients who were given 20 grains of potassium bromide and chloral hydrate in the 1st stage, and it will be observed that in neither case was there any appreciable change in the character of the uterine contractions; but in both cases the administration of the drug afforded the patient at least temporary relief from her suffering. One can only conclude that any beneficial action following the exhibition of potassium bromide and chloral hydrate is not due to its effect on the uterine contractions—in one case the agent may act by relieving pain and giving rest; in another by diminishing the resistance of the soft parts and removing nervous inhibition.

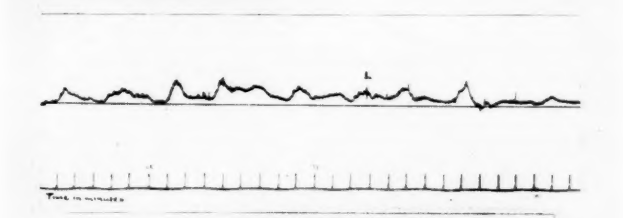
Morphia. Out of the welter of sedative drugs which may be and have been employed in obstetrics morphia emerges as one which has stood the test of time. Clinical experience with the administration of morphia during labour indicates that the action of the drug is variable. In one patient it has no effect on the progress of labour; in another it apparently hastens delivery; in a third it may retard the progress of labour for a short time; but in practically all cases the patient is made more comfortable and is given temporary relief from her suffering.

Generally speaking, experimental evidence regarding the action of this drug supports the view that in moderate doses it has little or no effect on the uterine contractions, and the several hysterographic observations on the human uterus in labour made by the investigator are in accord with this opinion. Figs. 35 and 35*a* illustrate an average effect following the injection of $\frac{1}{4}$ grain of morphia in the 1st stage of normal labour. The first effect noticed in the tracing is an increase of tone at point *b* and at *c* (approximately 20 minutes after injection) it can be appreciated that there is some decrease in the frequency of the contractions. This slight depression in the frequency of the contractions persists (for approximately 40 minutes) up to point *d* but thereafter the contractions return to their original frequency. There is little alteration in the intensity or the duration of the contractions. The important point to note is that, in this particular instance, following the administration of



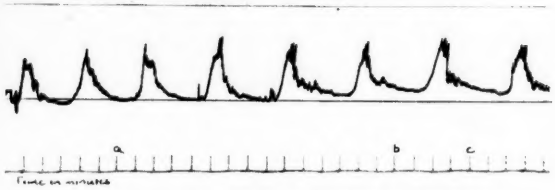
Potassium bromide + Chloral hydrate Normal first stage.
Primipara. Breech. Right sacro-anterior. Half dilatation.
Note (a) Potassium bromide + Chloral hydrate aa gr. 20.
No effect on progress of labour but patient more
comfortable, (F.M.) foetal movements.

FIG. 33



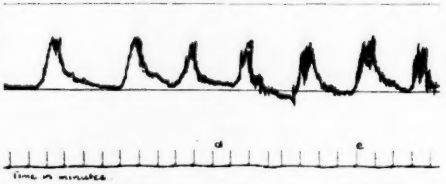
Potassium bromide + Chloral hydrate - Inert first stage.
Primipara. Vertex. Left occipito-anterior. Half dilatation.
Note (a) Potassium bromide + Chloral hydrate aa gr. 20,
(b) no effect on progress of labour but patient more
comfortable during pains, (L) laughing.

FIG. 34



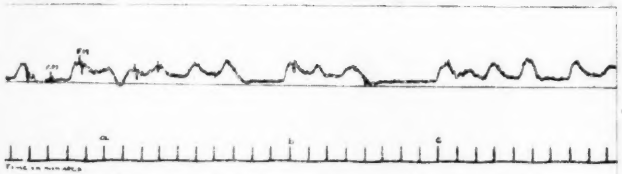
Morphia - Normal first stage. Primipara. Vertex. Left occipito-anterior. Half dilatation. Note (a) Morphia gr $\frac{1}{4}$, (b) increased tonicity, (c)decreased frequency of contractions, patient dozing between pains.

FIG. 35



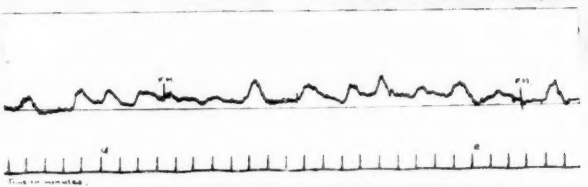
Morphia - Normal first stage.(continued). (d) patient wakeful, (e) full dilatation.

FIG. 35A



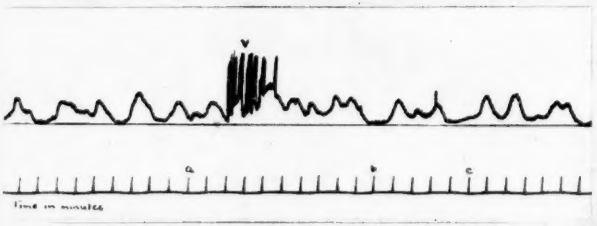
Morphia - Inert first stage.Primipara. Vertex. Right occipito-posterior. Three fingers dilatation. Note (a) Morphia gr.$\frac{1}{4}$, (b) patient more comfortable during and sleepy between pains, (c) increased tonicity, (F.M.) foetal movements.

FIG. 36



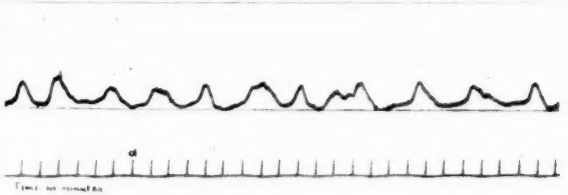
Morphia - Inert first stage.(continued).(d) depression of frequency and intensity of contractions and prolonged decrements, (e) patient wakeful, (F.M.) foetal movements.

FIG. 36A



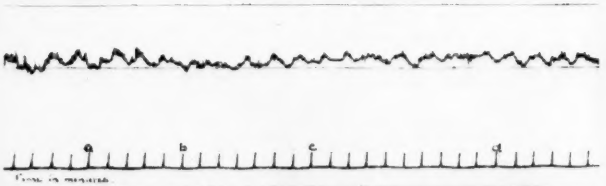
Morphia + Hyoscine - Normal first stage. Primipara. Vertex. Right occipito-anterior. Three fingers dilatation. Note (a) Morphia gr ½ + Hyoscine gr 1/100, (b) patient dozing, (c) decreased frequency of contractions, (V) vomiting.

FIG. 37



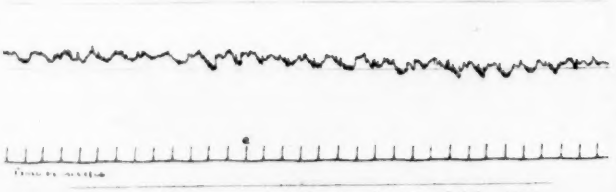
Morphia + Hyoscine - Normal first stage. (continued) (d) patient sleeping soundly.

FIG. 37A



Morphia + Hyoscine - Inert first stage. Primipara. Vertex. Right occipito-posterior. One finger dilatation. Note (a) Morphia gr ½ + Hyoscine gr 1/100, (b) decreased intensity of contractions, (c) increased tonicity, (d) patient dozing between pains.

FIG. 38



Morphia + Hyoscine - Inert first stage. (continued). (e) patient wakeful.

FIG. 38A

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morphia, the patient had an almost complete rest for 1 hour, during which time the labour progressed and the cervix dilated from half to full. Another example of the influence of morphia is seen in Figs. 36 and 36*a*. Here the contractions of the 1st stage were of a more inert type. At point *b* (10 minutes after the injection of $\frac{1}{4}$ grain of morphia) the patient was dozing, and at *c* an increase in the tonicity of the uterus is apparent. Subsequently there is some decrease in the intensity and frequency of the contractions with a tendency to prolongation of the decrements, and this is observed at *d* (50 minutes after injection). This period of depression of the uterine activity lasts approximately 45 minutes, when the tracing returns to the appearance presented before administration of the sedative. Morphia, then, has no marked or prolonged depressing influence on the uterine contractions—a slight diminution in the intensity and frequency of the contractions may be noticed 15 to 20 minutes after the injection but this is quite transient, and 40 to 45 minutes later the effect is no longer evident.

It is obvious that the clinical effects of morphia already deferred to cannot be completely explained on the basis of this slight and transient depression of uterine activity. In almost every case the injection of morphia during labour is followed by a period of rest, if not sleep, during which pain is largely obliterated and the patient is enabled to regain that tranquillity which she was in danger of losing before the administration of the sedative. Herein, probably, lies the main explanation of the undoubted value of morphia during labour. The stimulating action of the drug may be explained by a combination of effects. Often a patient who has been in labour a long time with little progress is given an injection of morphia, and shortly afterwards the cervix is fully dilated and delivery rapidly completed. This reaction is probably due to relaxation of the cervix and diminished resistance in the soft parts, increased tonicity of the uterine muscle combined with the increased tranquillity resulting from the abolition of pain.

Morphia and hyoscine. The use of this combination of drugs, first advocated under the name twilight sleep, is now well known. Its object in short is to produce analgesia during labour and amnesia afterwards, and there can be little doubt that properly applied it constitutes a most valuable adjunct to the practice of obstetrics. Briefly the method is to give an initial dose of morphia and hyoscine when the 1st stage of labour is well under way and subsequently small repeated doses of

hyoscine to maintain the narcosis. The patient sleeps during the interval; she wakes up with a pain and may be restless and even difficult to control, but sinks to sleep again when the pain passes off. Amnesia is usually complete, especially if a general anaesthetic has been employed during the actual delivery.

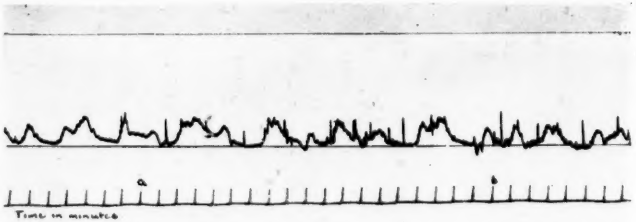
Hysterographically, the effect of morphia and hyoscine on the uterus in labour is that of morphia alone. There may be some slight and temporary depression of the uterine contractions, but in general the progress of labour is not interfered with to any appreciable degree. Figs. 37 and 37*a* represent tracings obtained during the normal 1st stage in a patient who was given 1/4th grain of morphia and 1/150th grain of hyoscine at point *a*. Some slight depression in the frequency and intensity of the contractions is noticed from point *c* (15 minutes after injection) onwards, but this is not obvious. The patient, however, was greatly relieved of her suffering and slept soundly in the intervals between pains. The effect of the administration of morphia and hyoscine in a more inert 1st stage is depicted in Figs. 38 and 38*a*.

Oxytocics.

Quinine. The oxytocic value of quinine is still a matter of discussion, but the consensus of opinion is that, on the whole, its action is undependable. Clinically, quinine usually has no apparent effect on uterine activity even when given in repeated doses, but occasionally it causes a fairly severe increase in the intensity and frequency of the uterine contractions.

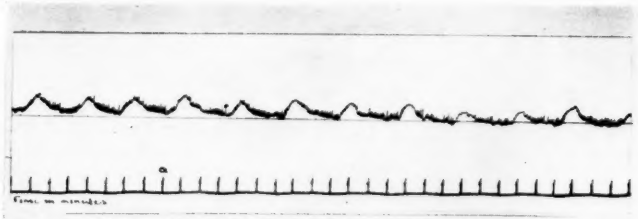
This clinical impression is borne out by the tracings obtained in this study. Figs. 39, 40, 41 and 42 are reproductions of tracings obtained in patients who were given 10 grains of quinine in the normal and inert 1st and 2nd stages respectively. In Figs. 40, 41 and 42 no effect can be demonstrated, but in Fig. 39 there is some improvement in the character of the contractions.

Pituitrin. The potency of the extract of the posterior lobe of the pituitary gland for stimulating uterine activity is a matter of common knowledge, and it is regarded by many as the most important factor in determining uterine contractions. It has comparatively little effect on the inactive uterus, but upon the parturient uterus its effects are quite dramatic. Its action is rapid, the contractions becoming extremely powerful and being increased in duration and frequency. The general opinion seems to be that, unlike ergot, pituitrin does not throw the uterus into tonic contraction but merely promotes an intermittent and



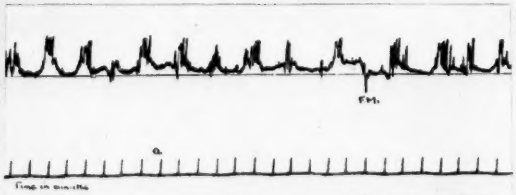
Quinine - Normal first stage. Primipara. Vertex. Right occipito-anterior. Two fingers dilatation. Note (a) Quinine gr 10, (b)slightly increased frequency of contractions.

FIG. 39



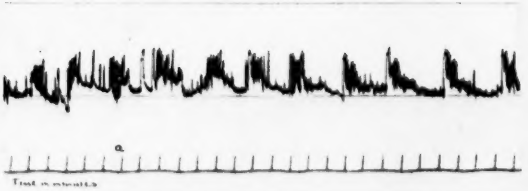
Quinine - Inert first stage. Multipara. Vertex. Right occipito-anterior. Three fingers dilatation. Note (a) quinine sulphate gr. 10, no effect on uterine contractions.

FIG. 40



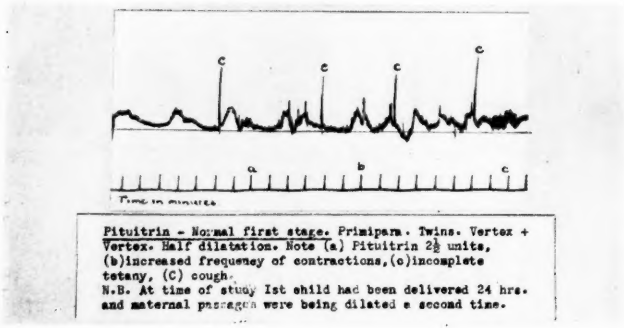
Quinine - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) quinine gr 10. No effect on uterine contractions, (F.M.) foetal movements.

FIG. 41



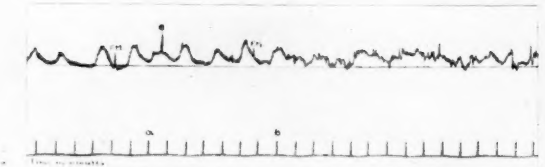
Quinine - Inert second stage. Primipara. Vertex. Right occipito-posterior. Note (a) quinine gr 10, No effect on uterine contractions.

FIG. 42



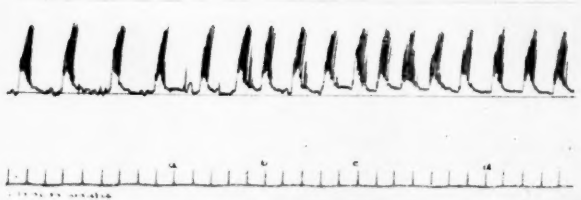
Pituitrin - Normal first stage. Primipara. Twins. Vertex + Vertex. Half dilatation. Note (a) Pituitrin 2½ units, (b)increased frequency of contractions,(c)incomplete tetany, (C) cough.
N.B. At time of study Ist child had been delivered 24 hrs. and maternal passages were being dilated a second time.

FIG. 43



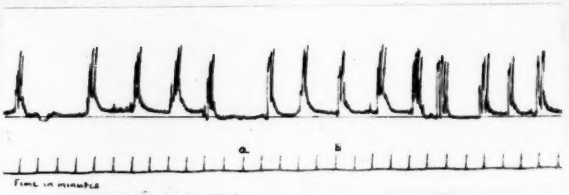
Pituitrin - Inert first stage. Primipara. Vertex. Right occipito-posterior. Three fingers dilatation. Note (a) pituitrin 2½ units, (b) incomplete tetany, patient uncomfortable, (C) cough, (F.M.) foetal movements.

FIG. 44



Pituitrin - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) Pituitrin 2½ units, (b)increased frequency and duration of contractions, (c) increased tonicity, (d) commencing relaxation.

FIG. 45



Pituitrin - Inert second stage. Primipara. Vertex. Left occipito-anterior. Note (a) Pituitrin 2½ units,(b)increased frequency of contractions.

FIG. 46

regular activity of that organ. The observations of several investigators, however, show that on occasion, at least, the uterus may be caused tetanically to contract by this drug. Many cases of rupture of the uterus have followed its indiscriminate use, and even in selected cases this accident has occasionally occurred. Obviously such a drug must be used with great caution. Its employment is strongly contra-indicated during the 1st and 2nd stages of labour if there is any disproportion, however slight, between the head and the pelvis, or any other cause of obstruction to the easy delivery of the head. During the 1st stage, when the uterine contractions are poor, it is of occasional value, but then only in small doses (e.g. $2\frac{1}{2}$ units) and given by an obstetrical expert well aware of its dangers. In cases in which delay occurs in the 2nd stage owing to weakness of the uterine action and the head of the child is low down, injection of a small dose of pituitrin is often followed by considerable stimulation of the uterine forces and delivery by the forceps avoided. The very properties which, in general, contra-indicate its use during the 1st and 2nd stages of labour make pituitrin an invaluable drug during and after the 3rd stage.

As a result of observations made for the purposes of this report the writer is of the opinion that the injection of pituitrin, even in small doses, is often followed by a tendency to tonic contraction of the uterus. The uterine contractions are markedly increased in intensity, duration and frequency, but the degree of relaxation between contractions is not complete—incomplete tetany. Four tracings are presented illustrating the action of pituitrin in the 1st and 2nd stages of labour, Figs. 43, 44, 45 and 46. In each case the injection of $2\frac{1}{2}$ units of the drug is followed in about 5 minutes by a quite definite alteration in the character of the contractions, affecting their intensity, frequency and duration. It will be noticed that the element of incomplete tetany is more evident in Figs. 43 and 44, representing the 1st stage, than in Figs. 45 and 46, representing the 2nd stage, and this may be of significance. Usually the effect of such a dose of pituitrin lasts about 30 minutes, but in Fig. 45 commencing relaxation is noticed at point *d* (17 minutes after injection).

Pitocin. In recent years the secretion of the posterior lobe of the pituitary gland has been separated into two principles—oxytocin and vasopressin; but whether the action of these principles on the uterus corresponds with those implied by their names is in some doubt, for certain observers have reported as

great an oxytocic effect with vasopressin as with oxytocin. In any event the oxytocic factor is nowadays commonly employed in obstetrics.

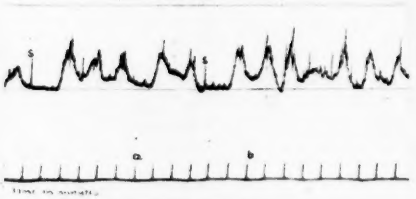
Several tracings made in patients who were given 2½ units of pitocin are shown in Figs. 47, 48, 49 and 50, and it can only be said that hysterographically there is no demonstrable difference between pituitrin and its oxytocic principle.

Thymophysin. Certain observations suggest that the thymus gland diminishes muscular fatigue and increases the rhythm and tone of uterine contractions. In the product thymophysin an attempt is made to combine these possible results with the well-known effects of pituitary extract. The combination, so far, has not been very extensively employed in this country, but elsewhere it has established for itself a considerable reputation.

The hysterographic studies made with this substance reveal that its action is practically identical with that of pituitary extract: it produces an increase in the frequency and intensity of the contractions but there is a tendency to incomplete relaxation between the contractions. Results with thymophysin are rather variable, and it does not appear to have any particular advantages over pituitrin. On the other hand, pituitrin is accurately standardized; its dangers in the 1st and 2nd stages and its virtues in the 3rd stage of labour are all equally well known. Figs. 51, 52, 53 and 54 are illustrations of more or less typical results following the administration of 0.2 c.c. of thymophysin.

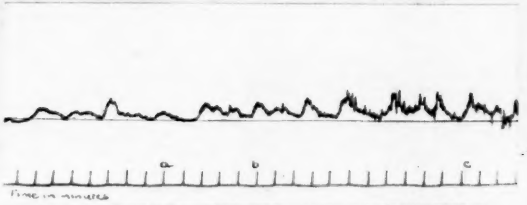
Oestrin. The relative importance of the part played by oestrin in controlling uterine activity is a matter of considerable discussion. It has been shown that the amount of oestrogenic hormone in circulation increases as pregnancy advances, but until the later weeks it is mostly in a combined or inactive form. The liberation of active oestrin immediately prior to the onset of labour is believed by many authorities to be responsible for the initiation of uterine contractions—probably by sensitizing the uterus to some other stimulus, mechanical, nervous or endocrine—and it is logical to assume that if this is true a sufficiency of oestrogenic hormone may be of prime importance in the maintenance of uterine activity. In any event, repeated attempts have been made in recent years to establish the value of oestrogenic therapy in cases of weak uterine action, and it must be said that some of the latest reports are at least promising.

The writer has made several hysterographic studies concerning the action of oestrogenic hormone during parturition with rather variable results. The preparation used was oestradiol



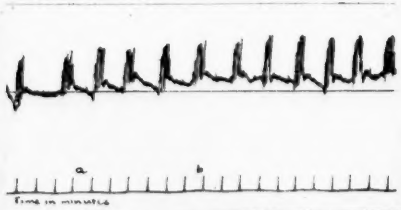
Pitocin - Normal first stage. Primipara. Vertex. Left occipito-anterior, Three quarters dilatation. Note (a) Pitocin 2½ units, (b) increased tonicity, (S) sigh.

FIG. 47



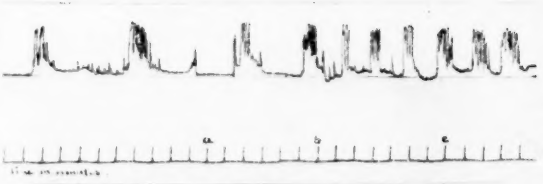
Pitocin - Inert first stage. Primipara. Vertex. Left occipito-anterior. Three fingers dilatation. Note (a) Pitocin 2½ units, (b) increased frequency, intensity and duration of contractions, (c) patient comfortable.

FIG. 48



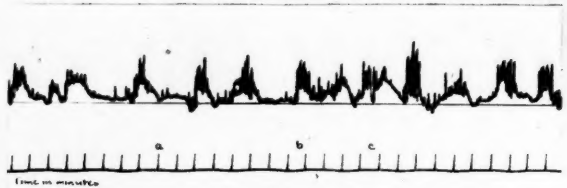
Pitocin - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) Pitocin 2½ units, (b) increased intensity and tonicity of contractions.

FIG. 49



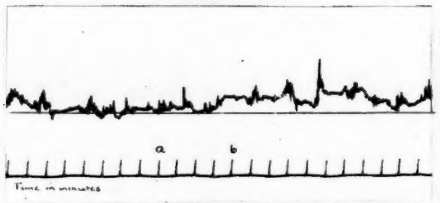
Pitocin - Inert second stage. Multipara. Vertex. Right occipito-anterior. Note (a) Pitocin 2½ units, (b) increased frequency and duration of contractions, (c) increased tonicity.

FIG. 50



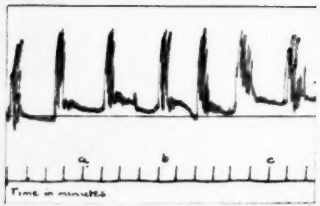
Thymophysin - Normal first stage. Primipara. Vertex. Right occipito-anterior. Almost full dilatation. Note (a) Thymophysin .2 cc.,(b)increased frequency of contractions, (c) incomplete relaxation.

FIG. 51



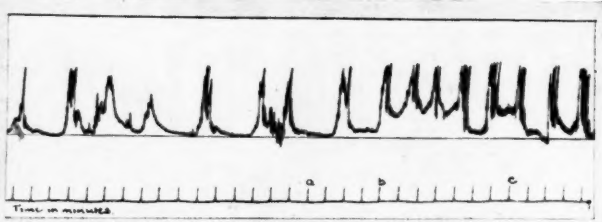
Thymophysin - Inert first stage. Primipara. Vertex. Left occipito-anterior. Half dilatation. Note (a) Thymophysin .2 cc.(b) increased intensity and tonicity of contractions.

FIG. 52



Thymophysin - Normal second stage.Primipara.Vertex.Right occipito-anterior. Note (a)Thymophysin .2 cc,(b)increased frequency of contractions,(c)increased tonicity.

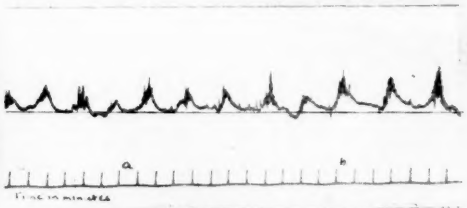
FIG. 53



Thymophysin - Inert second stage.Primipara. Vertex.Right occipito-anterior. Note (a)Thymophysin .2 cc,(b)increased frequency, duration and tonicity of contractions,(c)commencing relaxation.

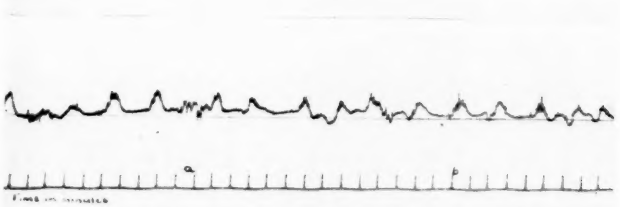
FIG. 54

FIG. 54



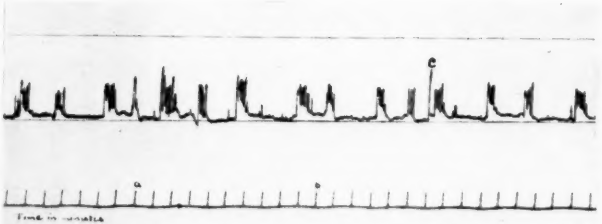
Oestrin - Normal first stage. Primipara. Vertex. Left occipito-anterior. Three fingers dilatation. Note (a)Oestrone benzoate in oil 2 mgm. (b) increased frequency and tonicity of contractions.

FIG. 55



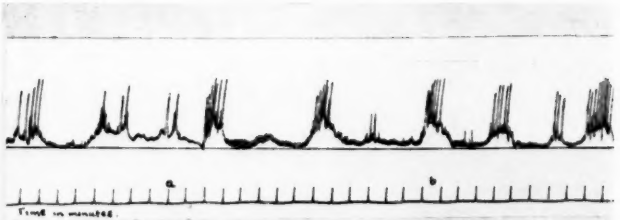
Oestrin - Inert first stage. Primipara. Vertex. Left occipito-anterior. Three fingers dilatation. Note (a) Oestrone benzoate in oil 2 mgm. (b)slightly increased frequency of contractions.

FIG. 56



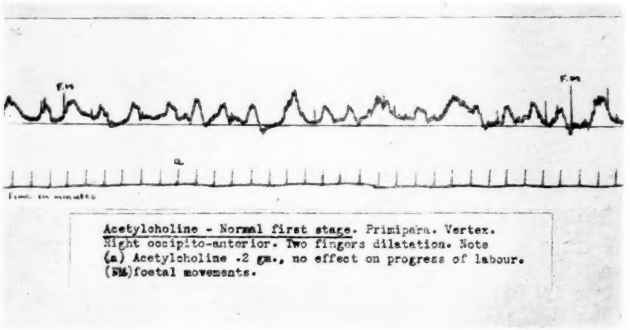
Oestrin - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) Oestrone benzoate in oil .2 gm. (b) No effect on uterine contractions, (C) cough.

FIG. 57



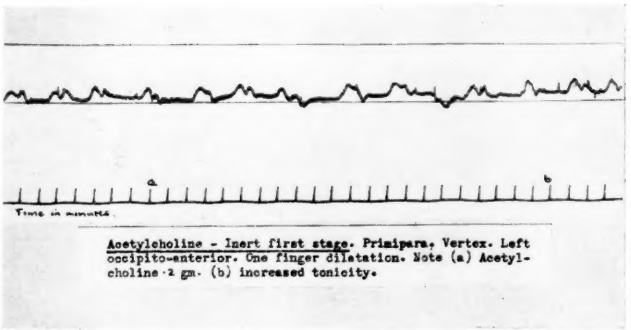
Oestrin - Inert second stage. Primipara. Vertex. Left occipito-anterior. Note (a) Oestrone benzoate in oil 2 mgm (b) increased frequency, intensity and duration of contractions.

FIG. 58



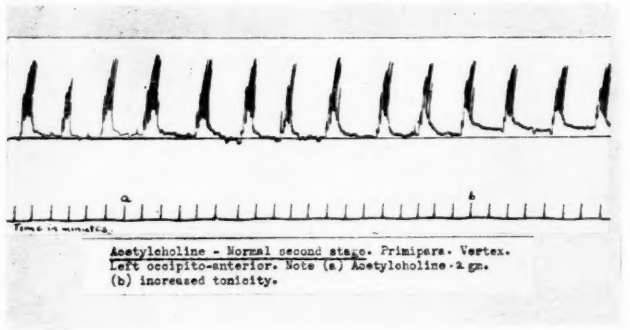
Acetylcholine - Normal first stage. Primipara. Vertex. Right occipito-anterior. Two fingers dilatation. Note (a) Acetylcholine .2 gm., no effect on progress of labour. (FM)foetal movements.

FIG. 59



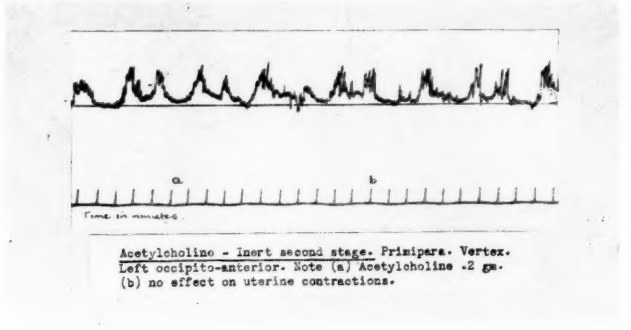
Acetylcholine - Inert first stage. Primipara. Vertex. Left occipito-anterior. One finger dilatation. Note (a) Acetylcholine .2 gm. (b) increased tonicity.

FIG. 60



Acetylcholine - Normal second stage. Primipara. Vertex. Left occipito-anterior. Note (a) Acetylcholine .2 gm. (b) increased tonicity.

FIG. 61



Acetylcholine - Inert second stage. Primipara. Vertex. Left occipito-anterior. Note (a) Acetylcholine .2 gm. (b) no effect on uterine contractions.

FIG. 62

benzoate in oil and it was injected in a dose of 2 mgm. (20,000 International Benzoate Units). In a number of cases the injection was followed by a quite definite improvement in the character of the contractions; in others there appeared to be no effect. One interesting point to note is the rapidity of the response when obtained. Experiments in animals suggest that oestrogenic therapy only stimulates uterine activity several hours after administration. Yet, although an oily solution was used which considerably delays absorption, a successful response was often noticed quite soon after injection. It can only be presumed that this response was produced by a small proportion of the total hormone given. Figs. 55, 56, 57 and 58 are average examples of tracings depicting the action of oestrin during the normal and inert 1st and 2nd stages of labour respectively and are self-explanatory.

Acetylcholine. Although a separate parasympathetic supply to the uterus has not been clearly demonstrated its existence has been commonly presumed. This presumption, together with an appreciation of the value of parasympathetic stimulation in such conditions as adynamic ileus, has led to attempts to stimulate the uterine action in labour by the administration of acetylcholine.

The several tracings made during the course of this investigation suggest that the effect of acetylcholine on the parturient uterus is variable. Occasionally it increases the intensity, duration and frequency of the contractions quite soon after injection and sometimes there is a definite increase in the tonicity of the uterus; in other cases a beneficial result is not demonstrable after administration. Figs. 59, 60, 61 and 62 are illustrations of some typical tracings obtained in patients who were given 0.2 gm. of acetylcholine at various stages and in various types of labour.

Summary.

The investigation of the problems of uterine inertia is beset by many pitfalls, not the least of which is the difficulty of measuring the forces of labour. As a possible solution of this difficulty a method of external hysterography is described which is applicable to and capable of yielding satisfactory recordings in all cases.

By this method many individual studies have been made and, while it is not pretended that the report presented is in any way exhaustive, an attempt is made to indicate the salient features of uterine activity in varying circumstances.

The general anaesthetics, gas and oxygen, ether and chloro-

form, in small amounts produce satisfactory analgesia without depressing the uterine activity. In larger amounts they depress the uterine contractions in direct proportion to the depth of anaesthesia produced.

The commonly employed analgesics and sedatives—potassium bromide and chloral hydrate, morphia, and morphia and hyoscine—exert little or no depressing influence on the uterus in labour, and their main value lies in the obliteration of pain and the increased tranquillity produced.

Of the oxytocics, quinine is undependable; pituitrin and its oxytocic principle, even in small amounts, markedly stimulate uterine activity, but have the disadvantage that they tend to produce a condition of incomplete tetany; thymophysin is less reliable than pituitrin and has no advantages over it; oestrin and acetylcholine quite definitely stimulate the parturient uterus in a proportion of cases, though not so dramatically as pituitrin.

I wish to acknowledge my indebtedness to Professor G. I. Strachan, Dr. R. G. Maliphant and Dr. M. D. Arwyn Evans for permission to investigate cases under their care, and to Mr. R. H. Linley, who is largely responsible for the photographic reproductions exhibited.

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An Investigation into the result of Operation in Genital Prolapse

BY

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Historical Survey.

UTERINE PROLAPSE has been recognized and treated for many generations. Hippocrates was familiar with the condition, and according to the comments of Francis Adams[1] in his translation of the seven books of Paulas Aegineta, "this complaint is particularly well treated of by the Father of Medicine. He has even described the case of complete procidentia, when, he says, the uterus hangs down like a scrotum". Paulas Aegineta believed that prolapse was rare, and he was rather sceptical of the occurrence of procidentia, which he described as "incredible". In the second century the aetiology of prolapse was well discussed by Aretaeus[2] who drew attention to the importance of difficult labour in causing relaxation of the uterine ligaments.

Although the pathology of the condition was well described by the ancients, the treatment they practised was more fragrant and picturesque than adequate. Hippocrates advocated cold applications and astringent lotions for local use, with cupping of the hypogastrium in severe cases. Aretaeus credited the uterus with voluntary motile power and stated that it "retreats inwardly if it be made to smell a foetid fumigation; and the woman also attracts it if she smells to fragrant odours". Woollen vaginal moulds were used at this time as a support for the uterus after a procidentia had been reduced, but it would appear that solid pessaries were not known. The introduction of these, and the various modifications which were devised, were the only advances made in treatment until comparatively recent times. Two hundred years ago controversy centred on the use and abuse of pessaries, of which the existing forms were condemned by John

Astruc[3] when he announced a recent advance as follows: "One made of Cork and covered over with Wax has been invented. This, being very pliable, permits the Patient to walk, exercise herself, nay to admit the Approach of Man, as well almost as ever". A few years later John Leake,[4] who was then physician to the Westminster Lying-in Hospital, condemned all pessaries as "those painful and indelicate instruments so often used with a bad effect for, instead of strengthening the weak part, they lay an additional stress upon it and consequently are highly improper". Progress was slow, however, and another 50 years passed with little alteration in the treatment of prolapse until the problem was at last attacked surgically.

The early methods of supporting the uterus by producing vaginal stenosis with caustics were succeeded by planned operations. At first a strip of vaginal mucous membrane was excised along the whole length of the canal, and the cut edges were sutured. Marshall Hall and Heming of Kentish Town[5] used this technique in 1831 and stated that the operation produced neither pain nor fever. Examination two years later showed the uterus and bladder to be in perfect position. It would appear that the operation was advocated first in 1823 by Romain Gerardin,[6] and was performed in Germany by Fricke and Diffenbach independently at least as early as 1831. The technique was advanced by Marion Sims[7] in 1858 when he instituted a V-shaped denudation of the anterior vaginal wall, and was further modified by Emmett, who also claimed perfect cures. Amputation of the vaginal cervix as practised by Huguier[8] and Scanzoni[9] was the next advance, but after Scanzoni had amputated the cervix on 16 occasions he stated that the operation was always dangerous. The value of an extensive posterior colporrhaphy was realized by Simon of Heidelberg[10] who designed his operation to support the cervix in a pouch at the vaginal vault. In over 30 cases Simon failed only once to effect a perfect cure, although his patients were poor peasants engaged in heavy work in the fields. It would appear that the credit for performing a combined anterior and posterior colporrhaphy must go to Melbourne, where Tracy[11] instituted the technique at the Women's Hospital and published an account of his operation in 1862. The next great advance was made in Manchester when, in 1888, Donald[12] combined a double colporrhaphy with amputation of the cervix. By removing a diamond-shaped area from the anterior vaginal wall and vault he displayed the para-cervical condensations of fascia with which he strengthened the repair.

Inglis Parsons,[16] who was Physician to the Chelsea Hospital for Women, devised a novel and apparently very successful technique which he practised first in 1897. He injected a quinine solution through the vaginal fornices into the cardinal ligaments. The fibrosis which followed the subsequent reaction was sufficient to correct the prolapse even in cases of procidentia. In his series of 93 cases treated by this method and including 19 of procidentia he claimed that 80 per cent were completely cured, and only one case was not improved. Moreover, 6 of his patients subsequently bore children without the prolapse recurring.

With the evolution of technique the principle of plastic vaginal operations for uterine descent has changed. Although originally prolapse was cured by producing such scarring or stenosis that recurrence was mechanically impossible, a constricted and functionless vagina is no longer the price of a successful repair but the evidence of one that is badly designed or unskilfully performed. The aim of the surgeon is to cure the prolapse and leave the vagina as normal as possible in length, diameter and mobility. Only when this aim is achieved can the operation be considered perfectly successful.

Investigation of Cases.

The desire to know how results would compare with this ideal was responsible for the investigations now recorded. It was evident early in the study of the series that to question and examine 100 patients was of more value than to analyse *questionnaires* from many times that number. Direct personal contact was particularly important in collecting data on the subject of post-operative dyspareunia. It also revealed, as recorded later, how a false impression of the success or failure of operation could frequently be obtained unless an examination was made.

The records of 488 operations for prolapse performed by eight gynaecological surgeons at the Chelsea Hospital for Women were studied, and there was no selection of individual cases. The series comprised all the consecutive prolapse cases treated surgically at the hospital by these eight surgeons during those years in which their individual records were investigated. The patients were requested to report for a progress examination, and appointments were so arranged over a period of 9 months that there was ample time for a detailed history and examination in each case. The longest interval between the times of operation and examination was 10 years and the shortest was 2 years. It was possible to trace 268 patients on whom 285 operations had been performed,

and the facts now recorded were collected from an analysis of the operative and post-operative histories and the findings at examination in this series. Operation had been performed for uterine or vaginal wall prolapse in all but 5 cases in which either a complete tear or a recto-vaginal fistula had been repaired.

Summary of Results.

The results are arranged in three groups. Group A includes only those operations which could be described as perfectly successful. Group B consists of the failures, although the term requires considerable qualification, as discussed later, and does not necessarily mean that the prolapse recurred. Group C contains the remainder, which consists of patients who, in many cases, were completely cured of their primary trouble. Many of these when first questioned stated that the operation had been a great success, but further questioning, or examination, revealed that the results were not perfect. It is the study of Groups B and C, therefore, that is most likely to produce improved results in any further series. An attempt has not been made to compare the results of operation in this series with those published by other authors: Fothergill,[13] Lacey,[14] Fletcher Shaw,[15] and others. It would be impossible to make a fair and adequate comparison, because no single operative technique was adopted and the collective results of eight surgeons were investigated. An attempt was not made to compare individual figures, and, moreover, the method of investigating this series and assessing results was different from that used by the writers mentioned.

As recorded in Table I, Group A consists of 165 cases, Group B

TABLE I.

Analysis of operative results.

Group.	Number of operations.	Percentage of total.
A	165	58
B	44	15
C	76	27

N.B.—Group A cases were perfect.
Group B cases were unsatisfactory.
Group C cases were satisfactory but not perfect. This classification is explained more fully in the text.

Number of recurrences 36, 13 per cent, of which 8 occurred after parturition, 22 per cent.

of 44, and Group C of 76. Table II summarizes the types of operation performed in each group, and it will be seen that on 177 occasions, constituting 63 per cent of the series, a combined anterior and posterior wall repair was performed. It is interesting to note that a posterior wall repair alone was required on 78 occasions as compared with the 21 on which an anterior one was necessary.

TABLE II.

Analysis of operation performed.

Group.	Combined anterior and posterior wall repair.	Anterior wall.	Posterior wall.	Inter-position.	Le Fort.	Ventral fixation.	
A	109	8	42	2	3	1	
B	24	7	11	0	2	0	
C	44	6	25	0	0	1	
Total	177	21	78	2	5	2	285

N.B.—Ventral fixation was combined with a plastic operation on 31 occasions. Twenty-two results were perfectly satisfactory and are included in Group A. It is interesting to note that all but 2 of these were performed before 1931, and most of them in 1928–1929. An abdominal operation for the correction of a retroversion was combined with a vaginal repair on 6 occasions, but these also were performed early in the series.

Detailed Analysis of Results.

GROUP A.

Concerning Group A, comment is unnecessary other than to repeat that it does not represent the total of satisfied patients, for many in Group C would be included under this heading. It includes only those who were assessed as being completely satisfactory when compared with the ideal standard already defined.

GROUP B.

Group B contains 44 failures in 37 patients on whom 53 operations were performed. It is significant that of the 16 repeated operations 7 again resulted in failure, an incidence of 44 per cent as compared with the 15 per cent of failure in the whole series. There are two possible explanations of this. Either the operation performed was not wisely chosen for the particular case, or

the surgeon was dealing with tissues of poor quality. This was undoubtedly the reason for some of the failures. A detailed analysis of this group is given in Table III. No sign of recurrence was found in 2 patients, in one of whom severe backache had been present since operation and had resulted in semi-invalidism. The condition was an orthopaedic one, but probably injury at the time of operation was responsible for it. The second patient complained of persisting discomfort after a rectocele had

TABLE III.

Analysis of Group B results.

(44 failures in 53 operations on 37 patients)

Complaint	Number
Anterior wall prolapse	16
Posterior wall prolapse	10
Anterior and posterior wall prolapse	4
Vault prolapse	8
Vault and anterior wall prolapse	1
Vault and posterior wall prolapse	2
Good anatomical result	2
Not examined (Letter from very dissatisfied patient) ...	1
Total	44

N.B.—Of these 44 failures 8 occurred after parturition.

been repaired, but examination revealed a most satisfactory anatomical result. Sixteen failures were due to the development of a cystocele, urethrocele, or both combined; but 5 of these were not recurrences, because at the primary operation a rectocele had been repaired and an anterior wall prolapse had not been detected. Ten failures were due to the development of a rectocele, but one of these was not a recurrence as only the anterior wall had been prolapsed at the time of the original operation. The corrected number of recurrent prolapses was thus 36, or 13 per cent of the series operated upon. Vault prolapse, either alone or combined with an anterior or posterior wall descent, accounted for 11 failures, and on 4 occasions both vaginal walls were prolapsed. It is interesting to note that 8 failures, or 18 per cent of the total, occurred after parturition. The shortest time in which symptoms recurred was immediately the patient left hospital and the longest was 8 years after operation.

GROUP C.

A summarized analysis of Group C is given in Table IV. The two most common complaints after operation were stress incontinence and dyspareunia. Of these two the former was the more common and the latter usually the more serious. The criticism may be made that the figures given cannot be regarded as accurate because of the difficulty in assessing the true extent of incapacity caused by these two complaints. It must be admitted that urinary control is not perfect in many women who have no evidence of

TABLE IV.

Analysis of Group C results.

Complaint	Number	Percentage of total series	
Stress incontinence, very slight ...	15	6	16
Stress incontinence, troublesome ...	28	10	
Dyspareunia	28	10	
Slight recurrence of dropping sensations	11	4	
Backache	6	2	
Vaginal discharge, slight in all cases ...	15	6	
Haemorrhoids	3	1	

prolapse, especially during exertion and when the bladder is distended; while dyspareunia may be a symptom of various disorders both mental and physical. In defence of the figures presented, however, it must be re-emphasized that the personal investigation of every case with the opportunity it provided of careful questioning and examination, was to exclude so far as possible errors of interpretation. Approximately 1,000 gynaecological patients who were examined during the months in which this investigation was made acted as a reasonable control series when it came to assessing the importance of symptoms.

DYSPAREUNIA.

Dyspareunia was complained of after operation by 25 per cent of all patients, and was permanent in 10 per cent. The first figure is much lower than one would expect and the second is much higher. In fact, there should not be any permanent dyspareunia. It is, of course, to be expected that when the vagina has been restored to a size and shape resembling that which existed at marriage there may be some initial difficulty in readjustment,

but this difficulty can be appreciably lessened if the nature of the operation is explained to the woman, or her husband, before she leaves hospital. The possible sequelae should be mentioned together with the methods best suited to avoid them. Every woman who undergoes a plastic vaginal repair is entitled to this advice, which unfortunately is denied to many. Several patients stated that there had been no attempt at intercourse after an operation performed years before because of advice allegedly given by a nurse during the time of convalescence in hospital. In other instances there had been such difficulty at the first attempt that it was claimed no further attempts had been made. As recorded in Table V, three of the 28 patients who complained of permanent

TABLE V.

Dyspareunia in Group C.

Cause	Number
Local cause not present	3
Local condition a doubtful cause	13
Stenosed introitus	5
General vaginal stenosis	1
Stricture at junction of middle and lower thirds of vagina	2
Tender perineal scar	1
Tender retroverted uterus	2
Senile vaginitis	1
Total	28

dyspareunia had no organic cause for the complaint and in each case it was possible to make a 2-finger examination without causing distress. In 13 of the remainder it was doubtful whether the operation was directly responsible, since examination gave the impression that the pains of which complaint was made were more functional than mechanical in origin. Such remarks as "it is probably just my age and my kidney what has dropped", and "it never does me any good, anyway", with which some patients qualified their complaint, were often a valuable index of the mental attitude of the patient to this aspect of her life. It is necessary to remember, however, that in all these cases, if the patient's evidence could be believed, the symptom was present for the first time following operation, and whatever the cause of the dyspareunia the potential domestic results were the same. Of the 12 patients in whom a definite mechanical cause was found, 5 had

a stenosed introitus, which in 3 was successfully remedied by a plastic enlargement. The remaining two, aged 51 and 60, requested admission for a similar operation. Intercourse was impossible in one case because of a generalized vaginal stenosis, and in two because of a tender stricture at the junction of the middle and lower thirds of the vagina. One patient had a tender perineal scar, two a retroverted tender uterus, and one, aged 51, had a severe degree of senile vaginitis. To summarize, an error in technique was responsible for a subsequent stenosis in 8 of the 28 cases and in 2 for a tender retroversion. At this stage it is only fair to state that several women volunteered the information that operation had improved their sex life, which had been better after the operation than ever before.

Stress Incontinence.

This was the most common complication, and occurred 43 times or in 16 per cent of the series. Fifteen patients described the complaint as slight and present only in cold weather or during severe coughing. Five stated that it was severe and a source of annoyance and discomfort, and 2 of these claimed that the disability was worse after operation than it had been before. The remaining 23 stated that incontinence was troublesome only at intervals. The good results that can on most occasions be obtained by a small plastic repair of a urethrocele and relaxed bladder-neck would suggest that the occurrence or persistence of stress incontinence after a prolapse operation is due to faulty technique in not extending the anterior colporrhaphy sufficiently far down the vaginal wall to permit of adequate support being given to the urethra itself.

Recurrent Symptoms of Prolapse.

A recurrent sensation of "something dropping" was complained of by 11 patients in Group C, all of whom described the symptom as slight. On examination no signs of prolapse were found in 4, 3 being gynaecologically healthy, while 1 was suffering from menopausal pruritus. Examination revealed only a slight bulging of the anterior wall during straining in each of the remaining 7 patients, of whom 5 were post-menopausal and 2 were menopausal. Three of these had not received any repair to the anterior wall at the primary operation. A colpoperineorrhaphy had been performed in each case, and in one this had been combined with a ventral fixation. Similarly in Group B,

as already recorded, there were 5 cases of recurrent symptoms due to an anterior wall prolapse when at the primary operation a rectocele had been repaired, and one instance of a rectocele following operation for cystocele. In a total of 9 cases, therefore, symptoms were due to weakness in a vaginal wall reported to be normal at the primary operation. In all of these the original repair was satisfactory at the time of the second examination, but in 6 of them a second operation was necessary to repair the subsequent prolapse of the opposite wall. In 5 cases this was the anterior wall and in one the posterior. This raises a point of considerable importance, for it may be argued that a more extensive operation, combining both an anterior and a posterior wall repair, would have prevented the onset of symptoms later and avoided the necessity of a second operation. Reference to Table II, however, will show that in Group A one wall only was repaired on 50 occasions, the anterior on 42, and the posterior on 8, without evidence of further trouble at the time of examination some years later. The table also shows that one wall was repaired on 99 occasions in the whole series. The fact that the opposite wall subsequently required attention on six occasions suggests that if a plastic repair is performed at the stage at which only a cystocele or a rectocele is present there is a risk of approximately 6 per cent of trouble occurring later because of prolapse of the remaining wall. From the figures given, the chance of this occurring would appear to be much greater when the primary operation is for a rectocele than when it is for a cystocele, but a careful analysis of the data available proves this to be incorrect. Although the relative incidence of secondary cystocele to rectocele was 5 to 1, the number of repairs of the posterior wall alone was 78 as compared with 21 of the anterior wall alone, a ratio of approximately 4 to 1. These results do, however, indicate the importance of making certain that there is no weakness of the opposite wall before deciding to perform a single colporrhaphy. It is reasonable to believe that the factors responsible for the descent of one wall have already weakened the remaining tissues in the pelvic floor and if the patient deferred her visit sufficiently long she would develop a more extensive prolapse.

Pregnancy after Operation.

Of those patients who had become pregnant after operation 19 were delivered vaginally, and although the number is too small to be conclusive, it is interesting to note that 11, or 58 per cent, remained perfectly satisfactory. In this connexion it is worth

repeating that 18 per cent of the failures in the whole series followed parturition. It is also apposite to quote the comments of Fothergill,[13] who wrote:

> "I formerly thought that an operation for prolapse should prevent recurrence even if the patient had one or more subsequent confinements, but we must remember that the arrangements which Nature has provided for the support of the pelvic viscera do not by any means always stand the test of pregnancy and labour. To expect from the surgeon arrangements superior to those designed by Almighty Providence, in cases in which these have already failed, is surely asking too much. All we can demand is that the new pelvic floor shall be as good as the original one and a little better if possible."

Operative and Post-Operative Mortality.

An analysis of the results of vaginal plastic operations would not be complete without reference to the operative and post-operative mortality. During the years from which this series was collected 1,310 consecutive repair operations were performed at the Chelsea Hospital for Women, and there were 11 deaths, a mortality of 0.8 per cent. The cause of death is recorded in Table VI and a study of this would suggest that a more careful selection

Table VI.

Operative mortality.

Number of deaths, 11. Number of cases, 1,310. 0.84 per cent.

Cause of death.	Number
Myocardial failure	4
Septicaemia	2
Pulmonary embolism	2
Peritonitis	1
Cerebral thrombosis	1
Death under anaesthesia	1
Total	11

of cases might have eliminated 5 or 6 from the series. The four patients who died of myocardial failure, the one who developed a cerebral thrombosis, and possibly the one who died under anaesthesia, might be considered as deaths that could possibly have been avoided. The fact that 3 of the fatal cases were due to infection is a reminder that although lethal sepsis is actually un-

common in vaginal surgery, it can be a relatively important cause of death in a large series. The ability of the vagina and perineum to withstand infection must not be overestimated.

During the year in which this investigation was made 269 prolapse operations were followed by one death, a mortality of 0.37 per cent, a figure which compares favourably with the mortality of 0.28 per cent for 1,073 non-abdominal operations performed at the hospital in the year 1937 to 1938. The death was due to myocardial failure, which, as shown by the figures presented, was the commonest cause of death in the whole series. This emphasizes the importance of making a careful examination of the cardio-vascular system in every patient before finally advising surgical treatment for prolapse. When unsuitable cases are thus eliminated the operative and post-operative mortality is extremely small and the prognosis for the future health and comfort of the patient is excellent.

Summary.

1. An historical survey is given of the evolution of technique in the treatment of genital prolapse.

2. The post-operative results of 285 operations performed 2 to 10 years ago are analysed.

3. Prolapse recurred in 13 per cent, 22 per cent of these being after parturition.

4. There was no recurrence of prolapse in 58 per cent of the patients who became pregnant after operation and who were delivered vaginally.

5. Stress incontinence of urine and dyspareunia were the most common post-operative complaints, and methods of avoiding them are discussed.

6. When prolapse was confined to one wall of the vagina at the time of operation in 6 per cent of cases a second operation was necessary years later for descent of the opposite wall.

7. Operative and post-operative mortality was 0.8 per cent and 0.37 per cent in two separate series analysed. The causes of death, and the methods of avoiding them, are discussed.

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Eclampsia

A Clinical and Biochemical Study

(*Part I was published in the June issue, page* 291)

PART II

BIOCHEMICAL INVESTIGATION OF ECLAMPSIA

BY

Dr. A. S. M. Nayar

Many years ago Zwiefel[19] called eclampsia "a disease of theories". Even to-day, in spite of the amount of work done, the aetiology of eclampsia is not definitely known. Biochemical investigations were carried out in 64 cases of eclampsia to see what light may be thrown by these studies. Since the incidence of eclampsia is increased as pregnancy approaches term, similar investigations were carried out in normal pregnant women at or about term and the results are presented. One hundred and three cases of normal pregnancy of various durations and 12 normal non-pregnant cases were investigated by the author in collaboration with Dr. E. Achyutha Menon (Antenatal Department) and these results are also incorporated. The investigations are taken one by one and discussed, and finally the whole work is examined together.

Blood-sugar. The majority of observers have reported fasting blood-sugar in pregnancy to be within normal limits.[20, 21, 22] Pillman-Williams and Wills[23] find that blood-sugar curves become lower as pregnancy advances. Herold[24] considers that the vagus and associated glands become more active in the later months of pregnancy and lead to hypoglycemia. Our results of blood-sugar estimations in 35 normal pregnancies at or about term show that 65.7 per cent of the patients have blood-sugar values below 70 mgs. per cent, i.e. definitely hypoglycemic, and 88.6 per cent have blood-sugar values below the normal average. (Graph I.) The mean average for normal pregnancy at term is found to be 64.5

mgs. per cent, and the maximum and minimum are given in Table I.

Regarding eclampsia Paul Titus and co-workers[25] find sharp falls in blood-sugar preceding fits, and wide fluctuations during the attack, ultimately leading to relative hypoglycemia, and therefore they recommend intravenous injection of glucose as a specific treatment in eclampsia and pre-eclampsia. Siegel and Wylie[26] support these observations and consider subnormal blood-sugar a characteristic of pre-eclampsia. Vera L. Kriegir[27] found hypoglycemia (i.e. below 80 mgs. per cent) in 33 per cent of the specimens examined in eclampsia. Mays and McCord[28] who studied blood-sugar readings throughout the convulsive stage in eclampsia, found marked variations in their readings and conclude that neither hyperglycemia nor hypoglycemia is characteristic of eclampsia. On the contrary, Stander[29] and Duncan[30] state that hyperglycemia is the rule in true eclampsia and advocate the use of insulin.

Our observations on 59 cases of eclampsia show (Graph I) that 52.6 per cent are definitely hypoglycemic, i.e. below 70 mgs. per cent. We have found only one patient with hyperglycemia at convulsive stage, and this patient was hypoglycemic at convalescence. (Table III.) We cannot, however, endorse the remark that hypoglycemia is characteristic of eclampsia in view of the fact that a much larger per cent of normal pregnancy at term was hypoglycemic. The maximal and minimal are also given in Table I.

We estimated in 14 cases of eclampsia blood-sugar at convulsive stage and at convalescence. One was hyperglycemic and therefore averages of 13 cases are given in Table II. Except that the minimal value is far below in convalescent series, an appreciable difference is not noted between the two conditions in their averages.

Blood-cholesterol. Hinglais and Govaerts[31] found high cholesterol content in the blood at term. Malpas[32] found an increasing curve of hyper-cholesterolemia in pregnancy rising from the 30th week onwards and reaching an average of 200 mgs. per cent at term. Bugnard, Colombies and Guilheim[33] found an increase in total cholesterol in later months of pregnancy. We estimated the total cholesterol in 30 pregnant women at or about term. The results are given in Table I and in Graph II. Total cholesterol was estimated in 62 cases of eclampsia, and from the results in Table I, maximal, minimal and average are all slightly below that of normal pregnancy. From Graph II it will be seen that 50.1 per cent of cases of normal pregnancy have blood-

cholesterol below 200 mg. per cent upper normal limit, and 49.9 per cent above it; while in eclampsia 56.4 per cent are below 200 mg. per cent and 43.6 per cent above it.

We estimated blood-cholesterol during eclampsia and convalescence in 8 cases besides the hyperglycemic case referred to. From Table II it will be observed that blood-cholesterol increases during convalescence as a rule. In the hyperglycemic patient, however, blood-cholesterol, which was very high at the convulsive stage, came down to nearly half its value (Table III).

Serum-calcium. Investigators of blood-serum-calcium in pregnancy present conflicting reports and contradictory data. Kehrer,[34] Mazzocco,[35] Krebs and Briggs[36] and Steward and Percival[37] report that the serum-calcium falls during the latter months of pregnancy. Deschamps[38] states that serum-calcium falls within normal limits in the first 9 lunar months of pregnancy and in the last month it is near the lower normal limit. On the other hand Underhill and Dimick,[39] Denis and King[40] did not find any change in serum-calcium level during pregnancy.

We have estimated the serum-calcium in 11 cases of normal pregnancy below 14 weeks, 52 cases between 15 to 28 weeks, 32 cases between 29 to 38 weeks and 40 cases at term. The averages, maxima and minima, are given in Tables IV–I, and percentages at different concentrations in Graph III. We find the averages are within normal limits. We may perhaps state that there is a tendency to a slight rise in the serum-calcium in the second trimester of pregnancy compared to the first, and a slight fall in the third trimester and a still slighter fall at term. (Tables I, IV and Graph III.)

In eclampsia also observations are divided regarding serum-calcium. Mitchell,[41] Brennan,[42] Krehbiel,[43] Kehrer[34] and Vozza[44] found hypocalcemia in eclampsia. Cantarrow[45] found a slight elevation in a limited series of cases. Advocates of the hypocalcemia theory of eclampsia have used calcium therapy, parathyroid therapy, or vitamin D therapy in the treatment of eclampsia. Some found encouraging results while others had disappointing results. In our series of 57 cases we find hypocalcemia, i.e., below 9 mgs. per cent, only in 12.4 per cent; serum-calcium within normal limits 9 to 11 mgs. per cent in 33.3 per cent, just above normal limit, 11 to 12 mgs. per cent, 21 per cent and above 12 mgs. per cent in 33.3 per cent. (Graph III.) Thus serum-calcium in eclampsia varies widely from frank hypocalcemia to definite hypercalcemia.

Serum-magnesium. Thus far no clinical significance has been

attached to the serum-magnesium estimation. Normal concentration of serum-magnesium may be considered (Bogert and Plass,[46] Denis,[47] Kramer and Tisdall[48] and Salvesen[49]) to be between 1 to 3 mgs. per 100 c.c. of serum. Denis,[50] Briggs[51] and Salvesen have shown that the serum-magnesium is practically uninfluenced by pathological conditions. Watchorn[52] has claimed that chronic infections are attended by increase in serum-magnesium, but the increase pointed out, viz., 3.5 mgs. per cent, has been found in normal condition.

The function of magnesium in the physiological economy of the body is imperfectly known. It is supposed to be similar to calcium and the most important action is supposed to be on the neuro-muscular system. Kruse and co-workers[53] have shown in their animal experiments that magnesium deficiency produces (*a*) characteristic symptoms of increased irritability of the nervous system, manifested in vaso-dilatation, hyper-excitability and tonic, clonic convulsions, and (*b*) constitutionally nutritive failure. One concomitant change observed by them was increase in total serum-cholesterol. No significant change in the serum-calcium or inorganic phosphate was observed.

In our 33 estimations of serum-magnesium of normal pregnancy we found the average value was 1.5 mgs. per cent, and from Graph IV we find 75.8 per cent lies within normal limits, 21.2 per cent below normal limits, and 3 per cent just above upper normal limit. We have given in Table V, 7 cases of magnesium deficiency with serum-calcium. We cannot make out any significant relation between serum-magnesium and total cholesterol or with other constituents.

The serum-magnesium was estimated in 56 cases of eclampsia. The average was within normal limits but slightly above that of normal pregnancy. The maximal and minimal were wider apart in eclampsia (Table I). In eclampsia also we did not observe any relation between magnesium and cholesterol and other constituents in magnesium deficiency cases (Table V). But of the two patients with hypermagnesemia (Table VI) one proved fatal, and the other developed sepsis in the puerperium.

Serum-sodium and potassium. Kramer and Tisdall[54] and Denis and Hobson[55] found that normal serum-sodium is 335 mgs. per cent, and potassium 19.5 to 20.5 mgs. per cent. Rosenbuck[56] found that in the last 3 months of pregnancy serum-sodium is diminished and chlorine is increased, and the diminution is more pronounced in eclampsia. But he found increased concentration of sodium in muscle, liver, spleen and kidney over that found in

normal pregnancy. Vozza[44] found the ration of Ca/K in normal pregnancy 1/1.8 and in eclampsia 1/2.2 to 1/2.9. Greenwald,[57] Denis and Von Meysenbug[58] produced convulsions in dogs by injection of sodium bicarbonate, sodium sulphate and sodium chloride. They found increased sodium concentration in serum by the injection. Greenwald thought that the convulsions are due to abnormal ration of $\frac{HCO_3}{NaHCO_3}$

The serum-sodium was estimated in 8 cases, and serum-potassium in 11 cases of normal pregnancy at term, and in 41 and 42 cases of eclampsia. The averages, maxima and minima, are given in Table I, and the different ranges of concentration in Graphs V and VI. It was found that while both serum-sodium and potassium were increased in pregnancy at term and in eclampsia, serum-sodium was much more in excess in eclampsia. Serum-potassium is increased above normal in eclampsia, but appears to be below that of normal pregnancy at term. From the graph it will be found that in eclampsia both sodium and potassium are widely distributed. The significance of the total base and these constituents in normal pregnancy and eclampsia will be considered later.

Serum-protein. The average normal serum-protein is 7.0 per cent according to Peters and Van Slyke.[59] Bruckman, d'Esopo and Peters[60] found low serum-protein in malnutritional oedema. During the last war Maver[61] showed that famine oedema was due to lack of proteins in the diet and the serum-protein was low. Frisch, Mendal and Peters[62] have produced oedema in white rats by low protein diet. Oard and Peters[63] observed that serum-protein falls during the first 6 months of pregnancy from an average of 7 per cent to 6.2 per cent, and a rise in the later months to reach an average of 6.9 per cent at term. We have estimated the serum-protein in 12 non-pregnant women, 10 pregnant women under 14 weeks, 39 pregnant women of 15 to 28 weeks, and 33 between 29 to 38 weeks. The average of these three periods are given in Table IV and the ranges in Graph VII. Perhaps we may state that in our groups the serum-protein is much diminished due to malnutrition and shows a progressive slight diminution as pregnancy advances without a rise in the third trimester. All our cases were poor hospital patients, evidently undernourished. The serum-protein was not estimated in eclampsia and pregnancy at term.

Inorganic phosphate. Denis and King,[40] Krebs and Briggs,[21] Oard and Peters[63] found that serum inorganic phosphate in normal

pregnancy lies within normal limits. We estimated serum inorganic phosphate in 11 normal pregnancies of under 14 weeks, 50 normal pregnancies of 15 to 28 weeks, and 37 of 29 to 38 weeks. The averages, maxima and minima, are given in Table IV. In these estimations Briggs' modification of the Bell and Doisy method was used. In pregnancies at term and eclampsia, Tisdall's colorimetric method was employed. Normal serum inorganic phosphate is 2 to 5 mgs. per cent. The results show that inorganic phosphate in normal pregnancies lies within normal limits, while at term it may be slightly raised. (Tables I, IV.)

Kydd and Peters[64] did not find any changes in inorganic phosphate in pregnancy toxæmias while Stander, Duncan and Scisson[30] observed that "serum phosphate is sometimes increased in toxæmias of pregnancy." Peters and co-workers[65] have found a moderate increase in the serum-phosphate in nephrotic types of nephritis, while abnormal increase of inorganic phosphate in chronic nephritis has been found by several workers ([51, 66, 55, 67, 68, 69]). It is well known that eclampsia is associated with nephrotic and nephritic types of renal disorders. In our series of 62 cases of eclampsia, the inorganic phosphate varied very widely (Graph VIII); 28.6 per cent of inorganic phosphate in eclampsia lies within normal limits, 28.6 per cent between 5 to 8 mgs. per cent, 29.9 per cent between 8 to 10 mgs. per cent. The correlation between inorganic phosphate and kidney function in these cases will be considered later.

Kidney function tests. Brown and Dodds[70] state that the majority of pregnant women exhibit kidney insufficiency when examined by laboratory methods. Adolph Bolinger and Earnlam,[71] using sodium thiosulphate excretion test, found a depression in the kidney function in later months of pregnancy. Janey and Walker,[72] using water excretion test, found that renal efficiency declines progressively during the last weeks of pregnancy. On the other hand Hurwitz and Ottaler[73] found urea clearance is higher than normal in pregnancy.

Urea clearance test. The urea clearance test of Van Slyke and co-workers ([74, 75, 76, 77]) has been claimed by Stander, Aston and Cadden,[78] Hurwitz and Ottaler[73] to be helpful in the differentiation of various renal disorders during pregnancy. We have estimated the urea clearance in normal pregnancy at term in 45 cases and the results are given in Table III and ranges of urea clearance in Graph IX and blood urea in Graph X. We find from Table VIII that the kidney efficiency in pregnancy at term is very much diminished, the average being 23.21 per cent of the average

normal. Though the average blood-urea is within normal limits, the urine-urea concentration and the urine volume are diminished and consequently clearance is much decreased. The normal urea clearance lies above 70 per cent of the average normal. W. Gelding and co-workers[79] observed the urea clearance in normal men is lowered by low protein diet, and Cope[80] found the same in nephritis. We have noticed that the urea clearance in normal persons with low protein diet is much lower than in persons with rich protein diet, and the lower limit of the normal variation may be extended down to 50 per cent of the average normal, instead of the usual 70 per cent. From Graph X it will be seen that 73.4 per cent of blood-ureas are within normal limits, but in the urea clearance Graph IX only 9.21 per cent are above the normal limit and 90.8 per cent of the urea clearances are below 50 per cent. of the average normal. Thus our results show that in pregnancy at term, judged by urea clearance, kidney efficiency is much depressed.

Regarding the renal function in eclampsia there are two schools of thought. Theobald[81] states that eclampsia cannot be accounted for by any functional or organic defects of the kidney. J. B. Llusia[82] states that blood urea is lower than normal in pregnancy and is still lower in eclampsia. On the other hand, Hurwitz and Ottaler[73] found the urea clearance is decreased in eclampsia and with improvement there was a rise in the urea clearance. A. Fruhin Sholz[83] observes that renal failure tends to initiate the trouble in toxaemias of pregnancy leading to hepatic failure. Nenoria Acosta Sisson,[84] in a clinico-pathological study of 38 cases of eclampsia, found chronic nephritis in 38.4 per cent patients. We estimated the urea clearance in 58 cases of eclampsia and found that the average blood-urea was just above the upper normal limit, Table VIII, but from the Graph X it will be found that 56.5 per cent of the blood-ureas were within normal limits, though only 16.1 per cent of the cases gave the urea clearance above the lower normal limit, Graph IX. The rest, 83.9 per cent, of the cases of urea clearance are below the normal limit. Thus a great majority of patients suffering from eclampsia have depressed kidney function, but when compared with normal pregnancy at term, though the average blood-urea is slightly above that of normal pregnancy at term, the average urine volume and urine-urea concentration and the average urea clearance are more than those of normal pregnancy; the percentage of kidney insufficiency is less than the percentage of that in normal pregnancy as judged by urea clearance.

Leon C. Chesley[85] considers from his observations that if the urine volume per hour is below 21 c.c., which he calls critical volume, the test should be discarded. If we apply this rule to our series, we find there are 12 patients in normal pregnancy and 18 patients in eclampsia in whom the hourly secretion is below this critical volume of 21 c.c. The averages, maxima and minima of urine volume, urine-urea concentration, blood-urea, urea clearance and percentage of average normal, of patients who are not affected by Chesley's critical volume are given in Table IX. Comparison of Tables VIII and IX convinces us that there is not much significant difference in the figures to justify Chesley's inference. From Graph XI and XII compared with IX and X, we find 73.4 per cent of blood-ureas in one and 84.4 per cent in the other are within normal limits in normal pregnancy, while 56.5 per cent and 59.7 per cent of blood-ureas of patients suffering from eclampsia are normal. Comparing the urea clearance we find 90.8 per cent and 87.5 per cent of normal pregnancy patients have kidney insufficiency, while 83.9 per cent and 79.4 per cent of those suffering from eclampsia are also similarly deficient.

We examined 9 cases of eclampsia by the urea clearance test during eclampsia and at convalescence. The averages, maxima and minima, of the 8 cases are given in Table X. One patient, whose kidney function was tolerably good for an eclampsia case, developed uterine sepsis during convalescence, and the kidney function, especially the urine-urea concentration, was thereby very much diminished. (Table X.) From Table X it is clear that the kidney function, as a general rule, improves with convalescence.

Filtration rate and creatinine clearance. Filtration rate developed by P. B. Rehberg[86] is not subject to the objections raised against urea clearance as a kidney function test. The objections raised against the urea clearance test are: (1) that the maximal and standard clearances are not comparable, except with the average normal of each. (2) It is not easy to understand why the urea concentration factor in standard urea clearance should be multiplied by the square root of the volume. Excretion of creatinine is found to be independent of the urine volume. Rehberg believed that the filtration rate, calculated by $F = U/B \times V$, represented the glomerular function. As the blood-creatinine value is small, he administered 3 gms. of creatinine in 50 c.c. of water by mouth, an hour before the test was started. At the start the bladder was emptied and a sample of blood was taken at the end of an hour and urine of one hour's secretion collected. Creatinine estima-

tions were made in both blood-plasmas and urine. The mean of the plasma values taken for blood-creatinine and filtration rate was calculated by the formula already stated. In normal persons Rehberg found values between 113 and 186 per min. after administration of creatinine and value below 100 c.c. was taken below normal. Rehberg's conception of filtration rate being a measure of the glomerular function was accepted by Hemingway[87] and Ellis and Weiss,[88] but questioned by Cope[89] and denied by Shannon, Jolliffe and Smith.[90] Its advantage over urea clearance is refuted by Hayman.[91] Hayman's objections are that the administration of creatinine by mouth is expensive, and analysis of the two samples of blood is laborious.

Grace Medes and Berglund[92] determined the minute filtration rate in 38 medical students without prior administration of creatinine. The range of filtration rate lay between 58 c.c. and 126 c.c., with a mean value of 88.6 c.c. The difference between the vastly different filtration rates without and with creatinine administration is not at present explicable. Medes and Berglund[92] state that " in normal individuals without creatinine injection it appears as if creatinine determines the rate of glomerular filtration and blood flow ". Hayman states that filtration rate below 41 per cent of the average normal is definitely abnormal, i.e. 41 per cent of 88.6, i.e. below 36.3 c.c., is definitely abnormal.

We estimated filtration rate without ingestion of creatinine in 43 normal pregnancies and 42 eclampsia cases. The averages, maxima and minima, are given in Table VIII from which it will be found that the blood-creatinine is higher in eclampsia patients than in normal pregnancy; the urine volume and urine creatinine are higher in eclampsia and consequently the average filtration rate is more than that of normal pregnancy though lower than that of the lower normal limit, i.e. 36.3 c.c., or say, in round figures, 40 c.c. From Graph XIII it will be seen that in 95.3 per cent of normal pregnancy kidney efficiency is below normal limits, and in 75.34 per cent of eclampsia cases also the same insufficiency prevails, as judged from filtration rate.

Chasis, Jolliffe and Smith,[93] Chasis and Jolliffe,[94] Jolliffe Shannon and Smith[95, 96] infer from their results that there is partial secretion of creatinine in renal tubules in man. Miller and Dubos[97] have demonstrated that all the chromogenic substance in normal serum is true creatinine. We have, therefore, estimated creatinine in one hour's urine and one blood-creatinine and calculated creatinine clearance exactly like urea clearance applying the formula $U/B \times \sqrt{V}$ when the volume is below 2 c.c. per minute

and UB/B when the volume is above 2 c.c. The results are incorporated in Table VIII and Graph XIV. Here also, taking 40 c.c. as the lower normal limit, we find in pregnancy at term 88.4 per cent are below lower normal limit and 80.0 per cent in eclampsia are similarly deficient.

Uric acid clearance. Williams,[98] Killian and Sherwin,[99] Krebs and Briggs,[21] King and Denis[100] and Plass[101] observed that uric acid remains normal throughout pregnancy. On the other hand Bunker and Mundell[102] and Harding, Allin and Van Wyck[103] found a rise in blood uric acid beginning in the later months of pregnancy and continuing progressively until labour is ended. We have estimated the blood uric acid clearance in 43 normal pregnancies and the results are summarized in Table VIII. Taking 2 to 5 mgs. per cent as normal for uric acid, it will be found that the blood uric acid in all cases lies within normal limits, but the average uric acid clearance is below the lower normal limit, 10 c.c. (10 to 20 c.c. being the normal limits), due to poor concentration of uric acid in urine and small urine volume. From Graph XV we see that 67.5 per cent of the cases are deficient in uric acid clearance in normal pregnancy.

Regarding eclampsia Peters and Van Slyke[104] state that blood uric acid is as a rule high in eclampsia or nephritis. Myers and co-workers[105, 106, 107] introduced the conception that blood uric acid is of diagnostic importance in nephritis; Myers's conclusions were supported by Watanab[108] and Banmann, Hansmann, Davis and Stevens.[109] Feinblatt,[110, 111] Follin and Denis,[112, 113] Woods,[114] and Holbrook and Haskins[115] do not consider that increased blood uric acid is a measure of renal insufficiency. Peters and Van Slyke,[116] it is stated, have given up in their laboratories the study of blood uric acid as a measure of renal insufficiency.

Caldwell and Lyle,[117] Harding and co-workers,[103] Killian and Sherwin,[99] King and Denis,[100] Plass,[101] Stander and co-workers,[30] found hyper-uricemia in toxaemias of pregnancy. So far as we know no one has attempted uric acid clearance to test renal insufficiency. We have estimated uric acid clearance in 61 cases of eclampsia. Our results are given in Table VIII and Graphs XV and XVI, from which we find blood uric acid is widely distributed; the average blood uric acid is just above the upper normal limit and 52.4 per cent of blood uric acid lies within normal limits, while 80.4 per cent show renal insufficiency as judged by uric acid clearance, and the average uric acid clearance also is much below the lower normal limit 10 c.c. and slightly below the average of

normal pregnancy. In uric acid clearance we used the same type of formulae used in urea clearance.

Chloride clearance. Chloride is a threshold substance. Disease of the tubules may affect the reabsorption of various threshold substances. We may find reabsorption of chloride affected by disease of tubules by finding it excreted in high concentration in urine in spite of low concentration in blood. On the other hand we may also find in some cases chloride reabsorbed with high blood chloride and low urine chloride. So the tubular function may be tested by comparison of chloride excretion with chloride level of blood. Therefore we estimated chloride clearance in 44 cases of normal pregnancy and 57 cases of eclampsia by using the same type of formulae used in urea clearance.

Normally whole blood contains 450 to 500 mgs. of chloride as NaCl per 100 c.c. of blood. Higher values have been found in nephritic conditions and eclampsia. Allen and Sherill[118] observed that hypertension had blood chloride above 620 mgs. per cent and about 61 per cent of the patients were either restored to normal or improved by salt restriction in diet. These results are refuted by Mosenthall[119] and O'Hare and Walker.[120] Nephrosis and nephritic stages of chronic haemorrhagic nephritis, characterized by profuse albuminuria, oedema and hypo-proteinemia, are often associated with high plasma chloride content (Gamble and others,[121] Major,[122] Peters and others[123]).

Athley and co-workers,[124] Marrack and Boone,[125] and Kydd and Peters[126] find eclampsia and toxaemias of pregnancy have no characteristic effect on chlorides. Harding and van Wyck[127] observe that hypertonic saline is harmful in toxaemias of later pregnancy. They consider that sodium chloride aggravates the condition. Maurice B. Strauss[128] produced signs and symptoms of toxaemias of pregnancy by administration of sodium chloride to pregnant women in the third trimester.

The results of our study are summarized in Table VIII. In both normal pregnancy at term and eclampsia the average blood chloride is above that of normal individuals, this being more so in eclampsia. But the urine chloride is much lower in eclampsia than that in normal pregnancy and consequently the average chloride clearance in eclampsia is much below that of normal pregnancy. Chloride is concentrated in urine normally two or three times. If we take 1.5 c.c. as lower normal limit of chloride clearance, both averages of eclampsia and normal pregnancy are below the lower normal limit. Examination of Graph XVII reveals that 72.7 per cent of the cases in normal pregnancy and 87.6 per cent of cases

of eclampsia have their chloride clearances below the lower normal limit, and consequently, as judged by chloride clearance, kidney insufficiency is marked out in eclampsia more prominently compared with normal pregnancy. (Graph XVII.) While Graph XVIII shows that 63.6 per cent in normal pregnancy and 62.5 per cent in eclampsia have blood chloride above the normal upper limit.

Discussion. Fasting blood-sugar estimations in our series show that in normal pregnancy at term 65.7 per cent, and in eclampsia 52.6 per cent, gave blood-sugars below 70 mgs. per cent. They did not present any symptoms of hypoglycemia. But in the literature we find several authors have reported sub-normal blood-sugars of 28 to 70 mgs. per cent without any signs.

Wauchope[129] has summarized the causes of hypoglycemia under four heads:

i. Excess of insulin:
   - (*a*) therapeutic injections,
   - (*b*) tumours and hyperplasia of the pancreas,
   - (*c*) functional hyper-insulism.

ii. Lack of opposing secretions:
   - (*a*) disease of supra-renal gland,
   - (*b*) pituitary tumours (posterior and anterior lobes),
   - (*c*) myxoedema.

iii. Lack of glycogen store:
   1. Destruction of stores as in
      - (*a*) disease of liver,
      - (*b*) wasting of muscle,
      - (*c*) abnormal excretions in renal glycosuria,

      or
   2. Active depletion of stores in
      - (*a*) muscular exercise,
      - (*b*) starvation.

iv. Interference with regulating centre:
   - (*a*) affections of the pons,
   - (*b*) overaction of the vagus.

Now, so far as pregnancy and eclampsia are concerned, hypoglycemia appears to be the result of (*i*) the lack of glycogen store, or (*ii*) overaction of the vagus. Schmidt[130] considers that the liver is unable to store normal quantities of glycogen during preg-

nancy, while eclampsia has been associated with liver damage in several reports. We have so far not got a sufficiently accurate laboratory method to measure hepatic insufficiency. However, as represented before, from our study we cannot endorse the opinion of other authors that hypoglycemia is characteristic of eclampsia. For we have found that a larger percentage of cases in normal pregnancy are also hypoglycemic. Stander and Duncan's statement that in true eclampsia hyperglycemia is the rule appears to be not confirmed by our investigations and the insulin therapy would, therefore, be positively dangerous. As to the overactivity of the vagus in pregnancy we have already cited Herold's views; confirmatory evidence about it has been lacking.

We may preface by stating that the average cholesterol content of the poor class of South Indians, the usual hospital class, is 150 mgs. per 100 c.c. A reference to Graph II will reveal that in normal pregnancy 86.6 per cent and in eclampsia 74.1 per cent have blood-cholesterol above the average value of 150 mgs. per cent. Therefore there is relative hypercholesterolemia both in pregnancy and in eclampsia. Several theories have been put forward for this hypercholesterolemia :

1. Suprarenal gland has been alleged to be the source of production and storage of cholesterol.

2. Theory of placental genesis has been put forward.

3. Necessity of hypercholesterolemia for the well-being of the mother by virtue of its anti-toxic and anti-haemolytic properties, is another plea put forward.

4. Hepatic insufficiency as cause of hypercholesterolemia is another suggestion.

From our figures we find one curious coincidence, that if we take 90 mg. per cent as the average blood-sugar, there is a certain amount of relation between the percentage of patients with blood-sugar below 90 mgs. per cent and blood-cholesterol above 150 mgs. per cent. (Table X.) We are, therefore, inclined to suggest that in normal pregnancy and eclampsia, hypoglycemia and hypercholesterolemia form a measure of hepatic insufficiency.

Total base. From the average figures for sodium, potassium, calcium (Table VII) and magnesium, we find that in normal pregnancy and eclampsia the total base is much more than that in non-pregnant normal, the figures for eclampsia being even more than that for normal pregnancy. Several workers have observed that there is a slight lowering of alkali reserve in later months of pregnancy. Whether this is due to a fall in blood carbon-dioxide or alkali deficit is debatable. Myers and co-workers[131] conclude from

their experiments and that of others, whose work supports their inference, that there is a mass of data to show that there is a fall of blood carbon-dioxide and a rise in *p*H during pregnancy. Kydd, Oard and Peters,[132] Stander and others,[133] and Kydd[134] find no change in the *p*H and Kydd and Peters[135] point out that there is no alkalosis in pregnancy and the fall in the alkali reserve and serum proteins in pregnancy is balanced by a fall in total base. Oard and Peters find total base in pregnancy is lowered by 5 per cent from the normal, i.e. 8 mm. Kydd and Peters found the chloride and phosphate normal and they do not find any accumulation of abnormal acid ions in the plasma.

Stander and others found in eclampsia markedly lowered carbon dioxide combining power. They find in eclampsia, which is associated with true acidosis, the total base is above that of normal pregnancy but below the level of non-pregnant normal. Stander and others' figures in normal pregnancy and eclampsia are given in Table VII. Total base shows 4 mm. more in eclampsia than in normal pregnancy; in our average it is 7 mm. more. Stander and others consider that uncompensated acidosis is the cause of death in eclampsia whereas in our series there is definite increase in total base, the main increase being in sodium and potassium. We find the ratio of $\frac{Na + K}{Ca + Mg}$ in normal pregnancy at term and eclampsia is greater than in normal, the ratio in eclampsia (Table XII) being, however, lower than that in normal pregnancy. Except total blood-chloride and serum inorganic phosphate we have not estimated the other anions. We feel, in the study of electrolyte content in eclampsia, there is a fair field for much more careful study which we hope to undertake later. Both inorganic phosphates and blood chlorides are increased in our series as stated already. We shall consider inorganic phosphate along with kidney function tests.

Kidney function tests. We propose to compare the four clearance tests we have done. We find from Table VIII that the blood-urea clearance and creatinine clearance give fairly the same percentage of kidney insufficiency in both pregnancy and eclampsia. Filtration rate gives a higher percentage than creatinine clearance. Probably creatinine and urea behave in the same way as regards kidney function. Both uric acid clearance and chloride clearance give a lower percentage in normal pregnancy than creatinine clearance and urea clearance, but in eclampsia nearly the same percentage as the other two. However, when we examine individual cases we find these clearances do not

all agree in the same direction. In Table XIV we have given 2 cases in which all clearance values are above lower normal limits. Also 8 cases are presented in which all clearances are below the lower normal limit. We have given another 9 cases in which the creatinine clearance is above the lower normal limit, while all or some of the other clearances are below their lower normal limits. In the six eclampsia patients all the other clearances—blood-urea clearance, uric acid clearance, and chloride clearance—are below their lower normal limits, but in normal pregnancy, the 3 patients with normal creatinine clearance, except the urea clearance which was below the lower normal limit, the other 2, uric acid clearance and chloride clearance are above the lower normal limit. It will be found from these figures creatinine clearance and filtration rates do not always agree.

SUMMARY.

1. We find that both in normal pregnancy at term and eclampsia there is hypoglycemia and hypercholesterolemia, probably suggestive of hepatic insufficiency.

2. The total base in our series is increased both in normal pregnancy and eclampsia, and more so in eclampsia, the increase being in Na + K.

3. The ration of $\frac{Na + K.}{Ca + Mg}$ is increased in both normal pregnancy and eclampsia, but this is less in eclampsia than that in normal pregnancy.

4. The great majority of cases of both normal pregnancy and eclampsia show kidney insufficiency as tested by the four clearances. The exact significance of the different clearance tests cannot at present be definitely stated.

CONCLUSION.

A comparative biochemical study of these patients has shown us some very interesting features. We prefer to discuss them under three heads—(1) the hepatic, (2) renal and mixed types together, and (3) the fatal cases.

The average blood-sugar in the normal pregnant woman, as shown before, is 64.48 mgs. per cent. In the hepatic and renal types the blood-sugar was within normal limits (90.08 and 82.21 mgs. per 100 c.c. respectively). The average blood-sugar among the fatal cases was 59.6 mgs. per cent, a definite hypoglycemia. This at least helps us to rule out the suggestion that there is a hyper-

glycemia in eclampsia, and the insulin treatment should not, therefore, be advocated. On the other hand, one should advocate intravenous glucose therapy in these cases; and this is now coming to the forefront more and more.

Serum sodium in the normal pregnant woman was found to be 375.5 mgs. per cent. In the hepatic group the average was 404.45 mgs. per cent, 421.3 mgs. per cent in the renal, and 365.6 mgs. per cent in the fatal cases.

Potassium in normal pregnancy is 40.85 mgs. per cent. In the hepatic type we found the average to be 29.34 mgs. per cent, 35.3 in the renal type, and 48.0 in the fatal cases. We find, therefore, a definite increase of the total bases sodium and potassium put together in the blood, and may we suggest that one should think twice before large doses of alkalis are administered to eclamptics.

The serum magnesium in normal pregnancies in our series was 1.51 mgs. per cent. In the hepatic group the average was 3.14 mgs. per cent; in the renal 1.59; in the fatal cases 4.5. In one fatal case it went up to 6.248 mgs. per cent. Thus we find an increase in the blood magnesium in the hepatic and fatal cases. The magnesium sulphate treatment of eclampsia is gaining more and more popularity. On the basis of these findings one wonders whether it could be used so indiscriminately. Would it not be better to restrict its use to those cases of renal eclampsia in which we find the magnesium is within normal limits? Again when magnesium is given intramuscularly does it increase its concentration in blood to any great extent? These are problems which are suggested for solution.

The inorganic phosphorus in the blood of a normal pregnant woman was 3.2 mgs. per cent. In the hepatic type it was 9.9; 5.2 in the renal type, and 9.1 in the fatal cases. We thus find an excess of phosphates in the hepatic and fatal cases.

The blood-calcium in all the three groups is within normal limits, 11.3, 11.1 and 10.8 mgs. per cent respectively. The calcium-phosphorus ratio is diminished and this is due to a rise in inorganic phosphorus, which seems to be of some prognostic significance.

The average blood-cholesterol for a normal pregnant woman was found to be 201.6 mgs. per cent. In hepatic eclampsia we found the average cholesterol as high as 260.05 mgs., while in the renal and fatal cases it was 212.18 and 205.8 respectively. We cannot draw any definite conclusions from this. The blood-chlorides show that the average values for the hepatic, renal and fatal cases were 541.4; 560.0, and 551.6 mgs. respectively. We

find a definite chloride retention in the hepatic and renal types. The average for normal pregnancy was 510.6. Perhaps it would be advisable to restrict the salt in eclampsia.

Urea. The average blood-urea in normal pregnancy was 44.0 mgs. per cent. In the renal type the average was 66.1, while in the hepatic and fatal cases it was 44.2 and 62.8 respectively. There seems to be some retention in the renal and fatal cases. The urea clearance value also shows that the percentage of average values was 32.1 for the hepatic type, and 29.18 per cent and 14 per cent for the renal and fatal cases respectively; the average for normal pregnancy being 23.24 per cent.

Uric acid. In the fatal cases, the average was 6.5 mgs. (10 mgs. maximum). In the hepatic type it was 5.3, and for the renal 4.7 mgs. The average for normal pregnancy was 3.15. All are agreed that a rise in the uric acid content is of bad prognostic significance.

Creatinine. 12.9 mgs. per cent was our average for our fatal cases, while it was 6.2 for the renal and hepatic types. In one fatal case it went up to 24 mgs. The average for normal pregnancy was 2.89 mgs. per cent. An increase of blood-creatinine is of grave significance.

From these observations we conclude:

1. Artificial rupture of membranes has a very definite place in the treatment of eclampsia. In our series the mortality was lowered from 16.7 per cent to 8.7 per cent.

2. It is suggested that eclampsia may be divided into renal, hepatic and mixed types.

3. Hepatic eclampsia is rare, but much more fatal than the other varieties. An attempt by biochemical investigations to separate these entities has shown that.

4. Hypoglycemia is marked in the fatal cases, suggesting intravenous glucose therapy.

5. Increase of inorganic phosphorus, uric acid, creatinine and magnesium are of grave prognostic significance.

6. There is an increase of total bases in the blood and so alkalis should be carefully administered.

7. Calcium behaves normally.

8. Hepatic eclampsia differs from the renal type in that there is an increase of magnesium, phosphorus, cholesterol and uric acid with a practically normal blood-urea and urea clearance.

9. The urea clearance value is very much diminished in the fatal and renal types of eclampsia.

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Graph I

Ranges of blood-sugar in mgs. per cent

	20 to 30	30 to 40	40 to 50	50 to 60	60 to 70	70 to 80	80 to 90	90 to 100	100 to 110	110 to 120	120 to 130	130 to 140
Normal pregnancy	% 2.8	% 11.4	% 22.9	% 5.7	% 22.9	% 8.4	% 14.3	% 5.7	...	% 2.8	...	% 2.8
			65.7 per cent.									
Eclampsia	3.4	5.1	11.9	17.0	15.2	20.3	15.2	8.5	1.7	...	1.7	...
			52.67 per cent.									

Graph II

Blood cholesterol

	50 to 100 mg. %	100 to 150 mg. %	150 to 200 mg. %	200 to 250 mg. %	250 to 300 mg. %	300 to 350 mg. %	350 to 400 mg. %	400 to 450 mg. %
Normal pregnancy	6.7	6.7	36.7	33.3	13.3	3.3	...	...
Eclampsia	4.8	2.1	30.6	30.6	9.7	1.6	...	1.6
					74.1 per cent.			

Graph III

Serum calcium

	5 to 7 mg. %	7 to 9 mg. %	9 to 11 mg. %	11 to 12 mg. %	12 to 13 mg. %	13 to 14 mg. %	14 to 15 mg. %	15 to 16 mg. %
Normal pregnancy								
1 to 14 wks.	...	9.1	36.4	45.4	9.1	...	...	...
15 to 28 wks.	...	1.9	36.6	19.2	42.3	...	...	...
29 to 38 wks.	...	3.1	37.5	28.1	31.3	...	...	...
Full term	5.0	22.5	55.0	12.5	2.5	2.5	...	...
Eclampsia	3.6	8.8	33.3	21.0	14.0	7.0	8.8	3.5
Non-pregnant, normal	...	8.3	33.3	16.7	41.7	...	...	...

GRAPH IV

Serum magnesium

	Below 1.0 per cent mg.	1 to 3	3 to 4	4 to 5	5 to 6	6 to 7	7 to 8
	%	%	%	%	%	%	%
Term, normal pregnancy	21.2	75.8	3.0	...	...	...	...
Eclampsia	16.1	75	3.6	1.8	...	...	3.6

GRAPH V

Serum sodium, mg. per cent

	250 to 300	300 to 350	350 to 400	400 to 450	450 to 500	500 to 550	550 to 600	600 to 650	650 to 700
	%	%	%	%	%	%	%	%	%
Normal pregnancy	12.5	50	25	...	...	...	...	...	...
Eclampsia	11.9	19.0	28.6	16.7	14.37	14	...	...	2.4

GRAPH VI

Serum potassium, mg. per cent

	15 to 20	20 to 25	25 to 30	30 to 40	40 to 50	50 to 60	60 to 100	100 to 150	150 to 200
Normal pregnancy	...	...	27.3	...	54.5	18.2	...	...	...
Eclampsia	15.9	25.0	6.8	29.6	9.1	4.5	4.5	2.3	2.3

GRAPH VII

Serum proteins—normal pregnancy and non-pregnant

	No. of estimations	3 to 4 mg. %	4 to 5 mg. %	5 to 6 mg. %	6 to 7 mg. %	7 to 8 mg. %	8 to 9 mg. %
1 to 14 wks. ...	10	10	50	30	...	10	...
15 to 28 wks. ...	39	25.6	61.5	5.1	5.1	2.6	...
29 wks. to term	33	42.4	42.4	6.1	6.1	3.0	...
Non-pregnant ...	12	41.7	33.4	8.3	8.3	8.3	...

Graph VIII

Serum inorganic phosphate

	Below 1 mg. %	1 to 3 mg. %	3 to 5 mg. %	5 to 8 mg. %	8 to 10 mg. %	10 to 13 mg. %
Normal pregnancy ...	...	...	47.1	52.9	...	...
Eclampsia	1.6	9.5	17.5	47.5	14.3	9.6

Graph IX

Blood urea clearance

	Below 1 c.c. %	1 to 5 c.c. %	5 to 15 c.c. %	15 to 25 c.c. %	25 to 40 c.c. %	40 to 55 c.c. %	55 to 70 c.c. %
Normal pregnancy ...		18.2	47.6	25	4.6	4.6	...
		90.8 per cent			9.2 per cent		
Eclampsia	3.2	6.5	48.4	25.8	12.9	1.6	1.6
		83.9 per cent			16.1 per cent		

Graph X

Blood urea, mg. per cent

	15 to 20 %	10 to 50 %	50 to 80 %	80 to 110 %	110 to 150 %	150 to 200 %	200 to 250 %
Normal pregnancy	2.2	71.2	17.7	6.7	2.2	...	...
			26.6 per cent				
Eclampsia	...	56.5	32.4	6.3	3.2	...	1.6
			43.5 per cent				

Graph XI

Blood urea clearance of cases with urine above critical values in c.c.

	Below 1 c.c. %	1 to 5 c.c. %	5 to 15 c.c. %	15 to 25 c.c. %	25 to 40 c.c. %	40 to 55 c.c. %	55 to 70 c.c. %
Normal pregnancy ...		15.6	37.5	34.4	6.2	6.2	...
		87.5 per cent			12.4 per cent		
Eclampsia	...	4.5	47.7	27.2	15.9	2.3	2.3
		79.4 per cent			20.5 per cent		

Graph XII

Blood urea of cases with urine volume above critical value

	15 to 20 %	20 to 50 %	50 to 80 %	80 to 110 %	110 to 150 %	150 to 200 %	200 to 250 %
Normal pregnancy	3.1	81.3	12.4	3.1	...	...	...
			15.5 per cent				
Eclampsia	...	59.5	34.0	4.2	...	...	2.1
			40.3 per cent				

Graph XIII

Filtration-rate $F\frac{U}{B} \times V$

	Below 1 c.c.	1 to 10 c.c.	10 to 20 c.c.	20 to 40 c.c.	40 to 70 c.c.	70 to 100 c.c.	100 to 120 c.c.
Normal pregnancy	...	30.3	48.8	16.2	4.6	...	...
Eclampsia	2.44	29.3	34.1	19.5	9.78	2.44	2.44

Graph XIV

Creatinine clearance

c.c. $= \frac{U}{B} \times \sqrt{v}$ below 2 c.c. $\frac{U}{B}$ xv above 2 c.c.

	Below 1 c.c.	1 to 10 c.c.	10 to 20 c.c.	20 to 40 c.c.	40 to 70 c.c.	70 to 100 c.c.	100 to 120 c.c.
Normal pregnancy	...	16.3	41.9	30.2	11.6	...	...
Eclampsia	...	22.5	27.5	30.0	17.5	2.3	...

Graph XV

Uric acid clearance: u.c. $= \frac{U}{B} \times \sqrt{v}$ below 2 c.c.; u.c. $= \frac{U}{B}$ xv above 2 c.c.

	Below 1 c.c.	1 to 5 c.c.	5 to 10 c.c.	10 to 20 c.c.	20 to 30 c.c.	30 to 40 c.c.	40 to 50 c.c.
Normal pregnancy	4.7	37.2	25.6	30.2	2.3	...	...
		67.5 per cent					
Eclampsia	8.2	49.2	23.0	16.4	1.6	...	1.6
		80.4 per cent					

GRAPH XVI

Blood uric acid

	Below 1 mg. %	1 to 3 mg. %	3 to 5 mg. %	5 to 7 mg. %	7 to 9 mg. %	9 to 10 mg. %
Normal pregnancy ...	...	44.2	55.8	...	...	...
Eclampsia	3.2	12.7	36.5	38.1	7.9	1.6
	52.4 per cent			47.6 per cent		

GRAPH XVII

Chloride clearance: $\begin{cases} \text{c.c. } \frac{U}{B} \text{ xv above 2 c.c.} \\ \text{c.c. } \frac{U}{B} \text{ x } \sqrt{\text{v}} \text{ below 2 c.c.} \end{cases}$

	Below 0.1 c.c.	0.1 to 0.5	0.5 to 1	1 to 1.5	1.5 to 2	2 to 2.5	2.5 to 3.5	3.5 to 4.5
Normal pregnancy	2.3	15.9	22.7	31.8	20.5	6.8	...	...
		72.7 per cent						
Eclampsia	...	40.3	29.8	17.5	3.5	5.3	...	3.6
		87.6 per cent						

GRAPH XVIII

Blood chloride

	250 to 350	350 to 450	450 to 550	550 to 650	650 to 750	750 to 850	850 to 950	950 to 1050
	%	%	%	%	%	%	%	%
Normal pregnancy	2.3	9.1	2.50	50.0	13.6	...	...	...
	36.4 per cent			63.6 per cent				
Eclampsia	...	...	37.5	42.2	14.0	4.7	...	1.6
					62.5 per cent			

TABLE I

Mgms. per 100 c.c.

	Normal pregnancy (Term)				Eclampsia			
	Number of cases	Maximum	Minimum	Average	Number of cases	Maximum	Minimum	Average
Blood-sugar	35	133.0	27.7	64.5	59	121.4	21.5	68.4
Blood-cholesterol	30	311.6	93.0	201.6	62	284.1	63.4	191.9
Serum calcium	40	14.4	6.2	10.7	57	16.7	5.2	11.2
Serum inorganic phosphate	34	7.8	3.6	5.4	63	12.34	1.0	6.3
Serum magnesium	33	3.6	0.3	1.5	56	7.9	0.2	2.1
Serum sodium	8	629.1	291.8	375.5	42	662.7	266.9	397.1
Serum potassium	11	54.6	26.6	40.8	44	200.0	15.9	37.7

TABLE II

Mgms. per 100 c.c.

	Eclampsia				Convalescence			
	Number of cases	Maximum	Minimum	Average	Number of cases	Maximum	Minimum	Average
Blood-sugar	13	104.7	55.0	69.4	13	94.6	29.5	68.3
Blood-cholesterol	8	249.0	177.8	210.1	8	287.4	218.6	222.0

TABLE III

A Case of Hyperglycemia. (*Case* 14)

Mgms. per 100 c.c.

Blood-sugar		Blood-cholesterol	
Eclampsia	Convalescence	Eclampsia	Convalescence
237.1	56.5	410.0	231.9

TABLE IV

		Pregnancy (normal).			Non-pregnant or normal.
		1 to 14 weeks	15 to 28 weeks	29 to 38 weeks	
Mgm. per 100 c.c. Serum calcium	No. of cases ...	11	52	32	12
	Maximum ...	12.4	12.6	12.6	12.9
	Minimum ...	7.8	9.0	8.6	8.0
	Average ...	10.5	11.3	11.1	11.2
Mgm. per 100 c.c. Serum inorg. phosp.	No. of cases ...	11	51	37	
	Maximum ...	3.5	4.0	3.9	...
	Minimum ...	1.3	1.5	1.7	...
	Average ...	2.4	2.3	2.3	...
Gm. per 100 c.c. Serum proteins	No. of cases ...	10	39	33	12
	Maximum ...	7.7	7.2	7.8	7.1
	Minimum ...	3.6	3.3	3.3	3.2
	Average ...	4.9	4.2	4.1	4.6

TABLE V

Magnesium deficiency. Mgm. per 100 c.c. of serum.

Case No.	Serum mg.	Serum Ca.	Blood ch'strol	Blood urea clearance	Case No.	Serum mg.	Serum Ca.	Blood ch'strol	Blood urea clearance	Result
				per cent.					per cent.	Baby and mother
11	0.7	9.9	218.9	16.1	31	0.6	11.5	191.8	34.8	well
18	0.9	11.2	171.6	18.4	25	0.3	11.7	192.2	22.6	,,
23	0.9	9.3	245.6	18.6	29	0.7	12.0	233.2	37.3	,,
29	0.3	10.8	166.5	22.9	26	0.8	12.7	169.5	19.1	,,
30	0.6	13.5	169.0	8.7	39	1.0	12.5	165.6	10.8	,,
35	1.0	11.7	192.3	16.4	40	1.0	10.5	185.9	23.6	,,
36	0.9	10.4	260.4	8.7	44	0.9	14.4	121.8	38.8	,,
					45	0.7	12.9	63.4	13.7	,,
					29	0.6	11.8	177.8	34.3	,,

TABLE VI

Hypermagnesiumia

Case No.	Serum mg.	Blood cholesterol	Blood urea clearance percentage	Albumin in urine	Number of fits	Puerperium
—	7.9	194.9	17.6	+++	12	Sepsis mother; baby well
38	7.3	273.2	*		16	Died undelivered

* no urine; suppression of urine.

TABLE VII

Average base content

	Normal pregnancy.				Eclampsia.				(normal) Non-pregnant	
	Mg. per 100 c.c.		Milli equivalent		Mg. per 100 c.c.		Milli equivalent		Results obtained	
	Results obtained	Stander, etc.	Results obtained	Stander, etc.	Results obtained	Stander, etc.	Results obtained	Stander, etc.	Mg. per 100 c.c.	Milli equivalent
Sodium ...	375.5	325	163.2	141.3	397.1	332.0	170.2	144.3	335	145.6
Potassium ...	40.3	21.2	10.42	5.4	37.7	21.3	9.6	5.4	20	5.1
Calcium ...	10.7	9.6	5.33	4.8	11.2	10.7	5.6	5.4	10	5.0
Magnesium ...	1.5	2.3	1.24	1.9	2.1	2.8	1.7	2.3	2	1.6
TOTAL BASE ...	—	—	180.2	153.4			187.1	157.4		157.3

TABLE VIII

	Normal pregnancy (term).			Eclampsia.		
	Max.	Min.	Aver.	Max.	Min.	Aver.
Volume of urine per hour in c.c	99	6	33.8	178	1	43.7
Urine urea in mg. per 100 c.c. ...	2167.0	145.3	771.8	2185	191.7	1004.6
Blood-urea in mg. per 100 c.c. ...	121.0	18.6	44.0	228.0	22.0	56.5
Stand./Max. clearance in c.c. ...	52.5	2.6	13.4	67.3	0.2	16.3
Percentage of average normal	97.2	4.8	23.2	89.7	0.3	28.2
Number of cases: Pregnancy, 45; eclampsia, 58.						
Volume of urine per hour in c.c	99	6	34	130	3	42.6
Urine creatinine in mg. per 100 c.c. ...	219.8	10	83.7	289.8	37.7	111.1
Blood creatinine in mg. per 100 c.c. ...	6.3	1.4	2.9	7.3	1.6	4.4
Filtration-rate in c.c.	41.9	2.6	14.9	118.8	0.8	22.2
Creatinine clearance in c.c. ...	55.2	3.0	21.4	98.7	3.4	20.2
Number of cases: Pregnancy, 43; eclampsia, 42.						
Volume of urine per hour in c.c.	99	6	33.8	178	2	44.3
Urine uric acid in mg. per 100 c.c. ...	133.4	4.2	36.3	163.2	3.6	36.3
Blood uric acid in mg. per 100 c.c. ...	4.0	1.6	3.1	7.9	0.8	5.0
Uric acid clearance in c.c. ...	23.7	0.9	7.7	29.9	0.4	6.7
Number of cases: Pregnancy, 43; eclampsia, 63.						
Volume of urine per hour in c.c.	99	6	33.8	178	2	43.9
Urine chloride in mg. per 100 c.c. ...	1828.0	26.3	1023.2	1313.0	106.0	602.5
Blood chloride in mg. per 100 c.c. ...	700.0	298.0	559.4	1015.0	450.0	582.8
Chloride clearance in c.c. ...	2.2	0.05	1.2	4.0	0.13	0.9
Number of cases: Pregnancy, 44; eclampsia, 57.						

TABLE IX

Cases with urine volume above 21 c.c. per hour.

	Normal pregnancy.			Eclampsia.		
No. of cases examined	32			44		
	Max.	Min.	Aver.	Max.	Min.	Aver.
Volume of urine per hour in c.c	99	21	40.6	178	21	57
Urine urea in mg. per 100 c.c.	2167	165.3	697.4	2185	192.3	966.1
Blood urea in mg. per 100 c.c.	121	18.6	38.7	228	22	57.4
Urea clearance in c.c.	52.5	2.6	15.5	67.3	3.6	18.9
Percentage of average normal	97.2	4.8	28.3	89.7	6.7	32.7

TABLE X

	Eclampsia			Convalescence			Sepsis Lakshmi	
No. of cases examined	8			8			Eclampsia 10.12.36	Convalescence 25.10.37
	Max.	Min.	Aver.	Max.	Min.	Aver.		
1 hour's urine in c.c. ...	84	2	48.6	162	8.9	50	87	78
Urine urea in mg. per 100 c.c.	2185	391.3	1249.2	2111	282.4	819.7	1530	122.7
Blood urea in mg. per 100 c.c.	68.7	33.1	48.6	45.3	22	32.5	48.1	39
Urea clearance in c.c. ...	23.5	5.9	14.1	48.6	7.8	25.6	26 5	3.6
Percentage of average normal	43.1	10.8	26.0	90.0	14.4	45.2	48.9	6.6

TABLE XI

	Percentage of cases with blood-sugar below 90 mg. per 100 c.c	Percentage of cases with cholesterol above 150 mg. per 100 c.c
Normal pregnancy ...	88.4	86.6
Eclampsia	88.1	72.5

TABLE XII

$$\frac{Na+k}{Ca+mg.}$$

	Na+k Milli-equivalent	Ca+mg. Milli-equivalent	$\frac{Na+k}{Ca+mg.}$
Normal non-pregnant	150.7	6.6	22.7
Normal pregnancy	173.6	6.6	26.4
Eclampsia	180.0	7.3	24.7

TABLE XIII

Percentage of cases below lower normal limit, and above 5 mg. of inorganic phosphate per 100 c.c.

	Urea clearance	Filtr'n-rate	Creatinine clearance	Uric acid clearance	Chloride clearance	Serum inor.phos. upper limit
Lower normal limit	25 c.c.	40 c.c.	40 c.c.	10 c.c.	1.5 c.c.	5 mg.
Normal pregnancy	90.8	95.3	88.4	67.5	72.7	52.9
Eclampsia	83.9	85.3	80.0	80.4	87.6	71.4

TABLE XIV

Comparison of kidney function tests

Case No.	Urea clearance in c.c.	Creatinine clearance in c.c.	Filtration rate in c.c.	Uric acid clearance in c.c.	Chloride clearance in c.c.	Nature of case	Inference
Lower normal limit	25	40	40	10	1.5	...	
2	52.5	40.8	.	11.7	1.55	Normal pregnancy	1. Clearance results similar
56	36.6	69.2	.	18.9	4.03	Eclampsia	2. Above lower normal limits
1	7.4	14.8	.	4.9	1.2	Normal pregnancy	All clearance values are below lower normal limits
2	6.9	7.2	.	9.3	0.6	,,	
3	2.6	21.1	.	9.2	0.8	,,	
9	3.0	15.3	.	3.8	0.05	,,	
18	12.3	16.8	.	3.1	1.2	Eclampsia	
20	11.9	16.6	.	2.4	0.9	,,	
21	9.5	6.2	.	0.5	1.0	,,	
22	11.4	8.6	.	0.6	1.3	,,	
25	12.2	55.5	65.7	4.0	0.2	Eclampsia	Creatinine clearance in all these cases above lower normal limits; most of other clearances below lower normal limits
48	9.8	43.3	26.8	9.1	0.85	,,	
52	11.1	44.2	33.3	1.5	0.74	,,	
39	5.8	56.1	57.1	6.0	0.42	,,	
54	21.0	63.6	80.5	8.6	0.64	,,	
63	8.7	47.5	31.9	3.9	0.34	,,	
6	19.5	42.3	25.6	14.3	1.9	Normal pregnancy	
10	22.3	55.2	41.6	15.3	1.8	,,	
27	9.1	42.2	23.7	17.2	2.2	,,	

Calcification of the Human Placenta

BY

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IT is generally agreed that the average duration of human pregnancy is 280 days from the first day of the last menstrual period. The possibility of a gestation period longer than this was totally denied before 1855. It is now recognized, however, that abnormal prolongation of gestation does occasionally occur, though the difficulty in clinical diagnosis of postmaturity before or after the birth of the child is well known, largely because conception does not always occur at mid-cycle and dates are, therefore, unreliable if considered alone. For the purpose of this paper a case was not accepted as postmature unless the following criteria were all present: (1) A gestation of more than 294 days from the first day of the last period. (Patients with doubtful menstrual history were excluded.) (2) A baby weighing more than $7\frac{1}{2}$ pounds. (3) Evidence of over-development of the child.

An examination of 3,339 consecutive labour-records has shown that when the above criteria are applied, the mortality rate for postmature infants is 7.9 per cent against that of 4.8 per cent for mature babies (premature infants under 5 pounds excluded). It has been suggested that the increased mortality-rate among postmature infants is due to degeneration of the placenta, and many textbooks (Teacher,[1] Kerr,[2] de Lee[3]) state that the postmature placenta calcifies, implying this to be a cause of foetal death. We have made a study of the degree of calcification in premature, mature and postmature placentae with the idea of finding out (i) whether degeneration and calcification are likely to be causes of foetal death, and (ii) whether calcification of the placenta might be used to assist in the diagnosis of postmaturity.

PRESENT INVESTIGATION.

Sixty-one placentae have been obtained and examined in the following ways: (*a*) by means of X-ray photographs, (*b*) chemically, (*c*) histologically.

The placentae were all from patients whose medical history could be followed and were classified into three different groups.

1. *Premature.* Twenty-one placentae from patients in whom the duration of pregnancy was less than 265 days from the first day of the last menstrual period (average 208 days), and the weight of the child less than 5½ pounds (average 3 pounds 10 ounces). (This cannot be considered a true average, since in 7 cases the foetus was so small that it was not weighed. These cases were not included in the average.)

2. *Normal.* Twenty-four placentae from patients in whom the duration of pregnancy was between 275 and 287 days (average 282 days) and the weight of the child between 5 and 9 pounds (average 7 pounds 14 ounces).

3. *Postmature.* Sixteen placentae from patients in whom the duration of pregnancy was over 294 days (average 300 days) and the weight of the child greater than 7 pounds 8 ounces (average 8 pounds 8 ounces).

Methods.

Jars containing formol saline prepared from calcium-free reagents and distilled water were distributed to the wards of this hospital, Queen Charlotte's Hospital and the City of London Maternity Hospital. After delivery the placenta was placed directly in one of these bottles, in which it was preserved till analysed in the following ways:

1. *X-rays.* After removal of the membranes and umbilical cord, each placenta was X-rayed. The calcium appeared as a fine granular deposit, in many cases distributed around the periphery of the individual cotyledons. As the observations were not capable of numerical expression, the X-ray plates were graded by means of individual judgment into five groups, namely, no calcification, slight, medium, much and very much. The method was quick and convenient.

2. *Chemical.* The placenta was weighed and a piece removed for section. The entire organ was then minced, well mixed in an enamel bowl and a 200-g. sample was placed in a tared dish and dried in the oven at 100°C. Throughout, great care was taken to wash all the utensils used only with distilled water.

When dry, the sample was re-weighed, then ground to a fine powder in a mortar. A 5-g. sample was taken for analysis and after washing it the percentage of calcium was determined by the oxalate method in a manner similar to that described by McCance and Shipp.[4]

Although the formol saline used as a preservative was carefully neutralized with caustic soda, this did not entirely prevent the removal of calcium from the placenta. The placenta is such a large organ that the preservative apparently does not permeate right through it sufficiently quickly to prevent some autolysis taking place. This is accompanied by the liberation of acids, which appear to dissolve out some of the calcium. The amount removed was found to depend on the length of time the placenta had remained in the jar and the degree of calcification of the organ. Accordingly the amount of calcium in the formol saline was determined and added to the amount found in the placenta.

Results.

These are given in Table I and show the amount of calcium found in the placentae by the two methods of estimation.

The X-ray plates were graded without reference to the chemical data and on the whole very good correlation between the two sets of results was obtained. This shows that the degree of calcification can be determined almost as reliably by an X-ray photograph of the placenta as by direct chemical analysis.

From the results shown in Table I, it appears that marked calcification of the placenta does not take place before the 38th week, but the amount of calcium found in the placenta after the 40th week (i.e. normal and postmature cases) varies very much. The average figures are 98 mg./100 g. and 123 mg./100 g. respectively (both very much higher than that of 31 mg. found for the premature placenta). By consideration of the standard deviations the difference between the average calcium content of the premature and normal placentae is shown to be statistically significant, as also is that between the premature and postmature placentae, but the difference between the normal and postmature placentae is not significant. A greater difference between the normal and postmature would have been expected from the popular theory that the postmature placenta calcifies. Moreover, examination of the results shows that only 50 per cent of the latter were definitely calcified and of these less than 25 per cent were heavily calcified, whereas many of the normals contained very large amounts of calcium and two contained more than any postmature placenta analysed in this series.

The results were further supported by a preliminary investigation, in which 100 placentae were examined by the X-ray method only. Neither series offers any support to the belief that the postmature placenta shows a great increase in calcification.

TABLE I.

The Calcium Content of the Human Placenta.

Premature			*Normal*			*Postmature*		
Duration of pregnancy, in days	X-ray appearance	Calcium content, mg/100g.	Duration of pregnancy, in days	X-ray appearance	Calcium content, mg/100g.	Duration of pregnancy, in days	X-ray appearance	Calcium content, mg/100g.
113	Nil	9	275	Medium	45	294	Slight	37
119	Nil	19	275	Very slight	36	294	Very slight	39
147	Nil	21	275	Medium	77	294	Very slight	58
147	Nil	26	276	Very slight	14	295	Medium	60
166	Nil	32	279	Much	91	295	Much	118
178	Nil	28	280	Nil	18	295	Much	183
184	Nil	54	281	Much	107	296	Very much	243
197	Nil	21	281	Medium	76	296	Very much	346
206	Nil	21	281	Slight	68	297	Very slight	37
210	Nil	37	282	Much	146	297	Nil	28
224	Nil	40	282	Very slight	18	298	Much	147
228	Nil	43	282	Medium	100	299	Slight	50
238	Nil	19	283	Medium	143	311	Much	114
241	Nil	20	284	Medium	77	312	Medium	75
245	Medium	76	285	Medium	50	313	Very much	404
250	Nil	21	285	Very slight	38	320	Slight	41
250	Nil	43	285	Nil	18			
250	Nil	42	285	Nil	66			
252	Nil	24	285	Medium	142			
254	Nil	24	285	Very much	510			
267	Very slight	24	286	Slight	50			
			286	Very much	410			
			286	Nil	17			
			286	Slight	41			
Average, 31 Standard deviation, 15			Average, 98 Standard deviation, 117			Average, 123 Standard deviation, 113		

Apart from the low calcium content of the premature placentae a correlation could not be found between the degree of calcification and the weight of the placenta or child.

Microscopical Examination.

Few studies of the postmature placenta have been recorded, though Ballantyne[5] mentioned the following changes: The villi showed very little syncytium, foetal endarteritis was common, calcification was present and the Whartonian jelly of the cord showed denser fibres.

A microscopical examination of the series of placentae described above was made and the changes found did not appear to be more marked in the postmature than in the ordinary placenta at term. The observations cannot claim to be of much value as it is impossible to examine more than a fragmentary part of such a large organ as the placenta. Especial attention was directed to the calcium deposits and these were only seen in areas where the villi had degenerated. The parts of the villi chiefly involved were those nearest to the maternal surface, i.e. those furthest away from the foetal blood-supply. The many small white flecks visible with the naked eye on the maternal aspect of the placenta correspond closely with the calcium deposits seen in the X-rays. These observations are supported by those of Schönig,[6] who investigated the distribution of calcium in the placenta by precipitation as calcium oxalate and examination of sections in polarized light. He found that in the early months of pregnancy, very small deposits were found in the sub-epithelial zone of active villi. After the 5th month calcium was not seen in the active part of the placenta, but a great increase in the total calcium content was noticed, as deposits were found in any area where degeneration of villi had occurred. This deposition indicated the amount of villous degeneration.

Discussion.

The large variation in the amount of calcium in both the normal and postmature groups of placentae excludes the possibility of using the degree of calcification as a guide to postmaturity.

A study of the placenta by the above methods has not given any real indication of its functional quality. The degenerative changes found in the postmature placentae do not appear sufficient to cause any great diminution of function. The placenta has a large reserve of functional activity and Stander[7] states that it can

support the life of the foetus even when half its substance has been destroyed. Maxwell[8] has reported the results of the Chinese practice of needling the placenta through the abdominal wall to procure miscarriage and mentions cases in which living children were later delivered, although large areas of the placenta had been separated by haemorrhage. Hence the presence of a few degenerative changes may mean very little.

TABLE II.

Duration of pregnancy	Weight of baby		X-ray appearance of placenta	Calcium content of placenta
Days	*pounds*	*ounces*		*mg.* / 100*g.*
307	6	12	Much	117
300	4	12	Very much	376

If a dead foetus is retained *in utero*, calcification of the placenta follows,[1] and this has sometimes been erroneously regarded as the cause of foetal death. Two such cases came to the notice of the authors during the present investigation (Table II) in which the baby was macerated and had evidently been dead for some days.

In this small series there was nothing to suggest that postmature infants die because of placental degeneration. There was only one still-birth among the cases with heavy calcification and in this case death was due to tentorial laceration. The cause of increased foetal mortality in postmature cases is probably disproportion due to increased foetal growth, and a study of case records supports this view.

SUMMARY.

1. A study of the calcium content of the placenta by two methods has shown that the degree of calcification can be determined as reliably by an X-ray photograph of the placenta as by direct chemical analysis.

2. The degree of calcification of the premature placenta was almost negligible, but varied a great deal in both normal and postmature cases. Large deposits of calcium were found in less than 50 per cent of the latter, but were also present in many of the normal placentae. This precludes the possibility of using the degree of calcification of the placenta in the diagnosis of postmaturity.

We wish to thank Mr. W. Gilliatt for suggesting this investigation, and Dr. R. A. McCance for his continued interest and advice.

We also wish to express our gratitude to the X-ray Department of King's College Hospital for their co-operation.

One of us (M.M.) is indebted to the Medical Research Council for a personal grant.

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Treatment of Retroversion of the Uterus

An Impression of the Present Position from an Analysis of the Cases Undergoing Operation at the Samaritan Hospital, London.

BY

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This investigation was made in order to see whether the operations for backward displacement of the uterus performed at the Samaritan Hospital, during the five-year period from 1933 to 1937 inclusive, have brought relief from the symptoms of which the patients complained.

Opinion regarding such a displacement has widely changed during the past quarter of a century. Operations for the correction of retroversion and retroflexion were among the commonest in gynaecology, while to-day one hears it said that the reputation of a hospital can be assessed in inverse ratio to the number of ventral suspensions performed.

It is inconceivable that all the operations performed in early days did not bring any benefit, otherwise their popularity must have died sooner and more readily, and since the pathology of women has not changed, operations performed for sound reasons with beneficial results then should also help to-day. The frequency of retroversion of the uterus is illustrated by Smith's[1] figures. He found that condition in 1,320 patients from a total of 5,412 examined, and in 600 of these there was no other pelvic abnormality.

The uterus is not fixed in its normal position of anteversion and anteflexion, being free to rotate about a transverse axis passing through its fixed supports, the cardinal ligaments and paracervical tissues. It is only when the uterus is found beyond the normal range of mobility, which is less than half a circle, that it may be said to be displaced.

While there is a number of women in whom the uterus has always been retroverted, in unmarried women this condition rarely gives rise to symptoms or requires treatment, and before

any abdominal pain can be attributed to malposition of the uterus all other possible causes such as chronic appendicular trouble or constipation must be eliminated. The part played by retrodisplacement in dysmenorrhoea in single girls is very difficult to assess, but it is certain that the displacement is seldom the whole factor. However, there are a few isolated cases in which, all other measures having failed, an operation for the correction of the position of the uterus brings relief.

In the majority, it is only when they marry that girls with a retroversion complain. In married nulliparous women, dyspareunia is the most definite symptom that can be attributed to a retroverted uterus, and this is especially noticeable when the ovaries are prolapsed. The relation between retroversion and conception and the course of pregnancy is far less definite. While it is difficult to believe that an active spermatozoon deposited in the upper regions of the vagina finds any difficulty in making its way to the external os, even if this is pointing upwards and forwards, nevertheless a relative degree of sterility is found in women with retroverted uteri. Similarly, there appears to be a greater tendency to early abortion than when the fundus lies well forward, although Wollner[2] found that abortion occurred just as frequently after correction of the malposition as before. It is in parous women that retroversion giving rise to symptoms occurs most frequently.

After childbirth it is common for the heavy, soft uterus to fall backwards into the pouch of Douglas, particularly when the mother has been allowed to lie supine for long periods during the puerperium. Of the well-known symptoms, backache, pelvic discomfort, menstrual disturbances and vaginal discharge, backache is by far the most constant, but before this is attributed to malposition of the uterus other causes of orthopaedic or arthritic nature must be excluded. If there are no symptoms treatment is not needed.

When the uterus is movable and can be replaced, prolonged massage, postural treatment and exercises will do good, but these methods are only applicable to those patients with the leisure and money to carry them out religiously.

Pessaries will not cure a retroversion of long standing, for after their use for many years the displacement recurs when they are removed, and an added disadvantage is that their presence tends to promote marital troubles.

Operations for the fixation of the uterus to the anterior abdominal wall have been largely abandoned because (1) the

fibrous band which forms where the uterus is attached to the peritoneum sometimes stretches and allows the uterus to revert to its former position, and (2) there are many cases on record in which a ventrally fixed uterus has given rise to trouble in labour. Two examples of the first accident were found in this follow-up. Many ingenious vaginal methods designed to fix the uterus forward or to pull the cervix backwards and so throw the fundus forward have been suggested, but are little used. Measures which employ a shortening of the round ligaments are the vogue to-day. Alexander Adams's extra-peritoneal shortening has now lost popularity because it does not allow a proper survey of the pelvic organs.

Gilliam's intraperitoneal shortening, or one of its modifications, is the favourite method, while the operation of passing a loop of round ligament through the broad ligament on each side of the uterus and fixing it behind in the form of a sling, described independently by Baldy and Webster, is the choice of some surgeons.

Holden[3] employs an elaboration of this method, in which he anchors the ovarian ligaments to the most lateral portion of the distal round ligament loop behind the uterus, and in addition shortens the utero-sacral ligaments.

Wollner emphasizes the need of care in each case, when employing Gilliam's technique, to select the proper distance for the round ligament loop from the uterus, and the proper site for fixation to the fascia. In the series analysed a modified Gilliam technique was employed in 112 cases, while Baldy Webster's operation was performed 6 times.

Letters were written to 248 patients who were operated upon at the Samaritan Hospital during the five-year period selected. Patients in whom some additional gross pathological condition was present for which surgery was indicated were not included, since a good result here could not be attributed to the ventral suspension, which formed only a part of the operation.

Replies were received from 118, of whom 98 were examined. Of those examined there were only 2 women in whom the uterus had again rotated backwards. A consideration of the effect which the operation had upon the particular symptoms follows:

Dyspareunia. Eighteen patients complained of dyspareunia and backache; 15 were completely cured, 1 was considerably improved, there was 1 failure and 1 died of an inter-current infection during the convalescence.

Dysmenorrhoea. Thirty patients complained of dysmenor-

rhoea, mostly of the congestive type in which the pain commenced before the period; 13 were cured, 13 were improved, and 4 derived no benefit.

Sterility. Fourteen patients were operated upon; in 7 the operation was successful and 7 have had no further pregnancy.

Abortion. There were 3 patients in whom abortion during the early months had occurred on more than one occasion, and one patient had aborted 4 times before the operation. Every one of these patients has since had a full-time child without added hormone therapy.

Menorrhagia. In 13 patients menorrhagia was the main symptom; 3 were cured, 7 were improved, and 3 failed.

Backache. Forty-nine patients had backache as one of the principal symptoms. In 21 operation cured the backache, 15 were improved and in 13 the backache persisted unchanged.

Leucorrhoea. Leucorrhoea was very marked in 2 patients, and both were improved by operation.

Abdominal pain was the sole complaint in one case and operation did not relieve the patient.

Feeling of pressure in the rectum was the complaint of 2 women. This symptom was improved in one operation and the other was no better.

Two young women complained of recurrent nausea, with occasional vomiting, headache, and a dragging pain in the lower abdomen, a syndrome described by Quinn,[4] and both were considerably relieved by operation.

Of the single women for whom Gilliam's operation was performed, backache was the indication in 4 patients, and 3 of these were cured. Six patients complained of dysmenorrhoea; 4 were cured, 1 was improved, and in 1 the operation was a failure.

In addition 5 patients were examined on whom Gilliam's operation had been performed as well as colpoperineorrhaphy, when on completion of the plastic repair the uterus, generally a bulky one, remained tilted backwards. These cases were entirely successful.

Two others are of particular interest: a single woman, aged 33, underwent a plastic operation for vaginal prolapse 10 years previously. When seen in 1935 she complained of backache and dysmenorrhoea and there was uterine descent on straining, without marked laxity of the vagina. Gilliam's operation has cured her.

A multipara, aged 40, who complained of backache and dragging in the left iliac fossa and had previously had an un-

successful colporrhaphy for a uterine prolapse without much cystocele and rectocele, still had uterine descent in 1934. Gilliam's operation and perineorrhaphy was performed, and when seen this time there was no descent and her backache had disappeared.

An analysis of the failures is most instructive:

1. A married woman, aged 30, with one child, complained of backache and stress incontinence. The operation brought no benefit; the backache was subsequently treated by an orthopaedic surgeon and cured by exercises and massage. She still has stress incontinence and a cystocele is present.

2. A single girl, aged 24, complained of backache and menorrhagia for 2 years. Her symptoms have returned and a heavy, enlarged uterus is now completely retroverted and the ovaries are prolapsed.

3. A married woman, aged 38, with no children, complained of backache, dyspareunia and dysmenorrhoea (the pain in both the latter symptoms being in her back); after ventral suspension had failed she underwent orthopaedic treatment and is now better.

4. A married woman, aged 34, complained of pain in the left loin. The pain is still present and is situated around her left kidney and probably bears no relation to her pelvic organs.

5. A married woman, aged 33, complained of irregular menstruation, dysmenorrhoea, menorrhagia and epileptic fits at her periods. She is rather worse after her operation, but is mentally unsuitable for any surgery, except emergency.

6. A married woman, aged 32, complained of backache, frequency of micturition and dysmenorrhoea. Operation unsuccessful; the frequency of micturition was subsequently proved to be due to a bacillus coli urinary infection; her backache was probably due to cystitis.

7. A married woman complained of backache and abdominal pain. The result mechanically was a success, but the symptoms are as bad as before. Her abdominal pain seems too high for a pelvic cause.

8. A married woman, aged 40, complained of backache and leucorrhoea. The patient had a small mobile uterus which now lies well forward, but her symptoms remain the same.

9. A married woman, aged 27, complained of backache, vomiting and abdominal pain. She is rather worse after the operation.

10. A married woman, aged 46, one child, complained of backache. No improvement.

11. A married woman, aged 33, complained of backache, abdominal pain and menorrhagia. No benefit.

12. A married woman, aged 31, complained of bearing down feeling and menorrhagia. No better at all.

There were several more unsuccessful cases in which the indications appeared definite, but improvement in the symptoms did not follow. One merits detail. A married woman, aged 34,

complained of dysmenorrhoea and 8 years' sterility. She had a large uterus prolapsed on to the ovaries and Fallopian tubes. Abdominal insufflation under vision was carried out and the gas would not pass while the uterus was lying back, but did pass when the uterus was lifted forward. Her dysmenorrhoea was relieved by Gilliam's operation but she has not become pregnant. Another case is rather interesting. A married woman complained of leucorrhoea, backache and pain in the left iliac fossa. She reports great improvement since the operation, but the uterus is still retroverted. The lesson from this is that the psychological effect of the operation, together with rest in bed and good living which follow it, cannot be discounted when assessing the result of an operation performed only for the correction of an anatomical malposition and which can never be deemed essential for a continued existence.

It is seen, therefore, that some of these cases are failures because the indications were inconclusive, while in others subsequent developments showed the existence of a definite non-gynaecological pathology.

All the patients examined were carefully questioned with reference to any symptoms that could be attributed to the operation itself, and 10 patients had noticed a dragging sensation on one or the other side at the site where the round ligament was fixed to the abdominal wall, but in only one was this symptom severe. Various minor differences in technique were employed by the several operators whose cases have been investigated, and there is no evidence that a non-absorbable suture is better than catgut for fixing the round ligament to the rectus sheath. Both the mechanical failures occurred in cases in which thread was used for this purpose. The method of suturing the two loops of round ligament to each other superficial to the rectus sheath is criticized on the grounds of the post-operative pain it may cause, but there is no evidence from this series to support such a criticsm. The 6 patients for whom Baldy Webster's technique was used all now possess an anteverted uterus.

Conclusions.

1. The patient is treated for her symptoms and not for the position of her womb, but when symptoms are present and other possible causes for these symptoms have been excluded, there is still a place for a ventral suspension operation in carefully-selected cases.

2. A cure is fairly certain for dypareunia associated with a tender, retroverted uterus and prolapsed ovaries.

3. To cure prolapse when there is a bulky, retroverted uterus, Gilliam's operation may be necessary as well as colpoperineorrhaphy.

4. Gilliam's operation should succeed myomectomy when the primary incision in the uterus is anterior, unless the uterus lies right forward without support.

5. When retroversion is part of general visceroptosis Gilliam's operation will almost certainly fail.

6. It is most important to avoid performing the operation for symptoms which could not possibly be caused by retroversion. It is very difficult for a uterus of normal size to cause either frequency of micturition from irritation of the bladder by the anteriorly directed cervix, or pressure symptoms in the rectum by the retroverted fundus.

My thanks are due to Mr. Clifford White, F.R.C.S., Senior Surgeon, Samaritan Hospital, London, for permission to publish this report.

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Desmoblastoma Ovarii Malignum

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THE ovarian tumour now to be described is an exceedingly rare type of ovarian tumour to which Schiller[1] (1934) has given the name of "Desmoblastoma ovarii malignum". In his book *Pathologie und Klinik der Granulosazelltumoren* he devotes a chapter to three of these tumours, the chapter being entitled "Granulosazellähnliche Mischtumoren mit Knorpelbildung" (granulosa cell-like tumours with cartilage formation). Cartilage in ovarian tumours is rare apart from its occurrence in greater or lesser amounts in cystic or solid teratomata. Jung[2] described a case which is often quoted under the title of "Enchondroma of the ovary". He quotes two cases, one reported by Kiwisch and one by Reiss, but these were considered by Pfannenstiel to be doubtful; he thought that the case described by Reiss was a malignant myxomatous mixed tumour which should be reckoned as a teratoma.

The tumour here described is very rich in cartilage and appears to be very similar histologically to Jung's case and also closely resembles Schiller's three cases.

Jung's case is as follows:

A 48-year 7-para was admitted on account of irregular and severe uterine haemorrhage, retention of urine, pains in body and back, loss of sleep and appetite. Hysterectomy was performed and a large globular tumour of the left ovary was removed and also half the right ovary. Numerous peritoneal adhesions caused trouble. The patient returned to hospital 7 months later looking cachectic and complaining of a purulent vaginal discharge, abdominal distension, breathlessness, and headache. It was found that a fistula had developed and on account of intestinal obstruction another operation was performed when over a kilogram of necrotic tumour tissue was removed which had infiltrated the pelvic tissues but had remained extra-peritoneal.

The patient died one month later from peritonitis. Histological examination of the primary tumour showed that it was composed of three kinds of tissue:

1. A myxomatous connective tissue poor in cells.
2. A sarcoma-like tissue consisting of large cells.
3. Small islands of typical hyaline cartilage.

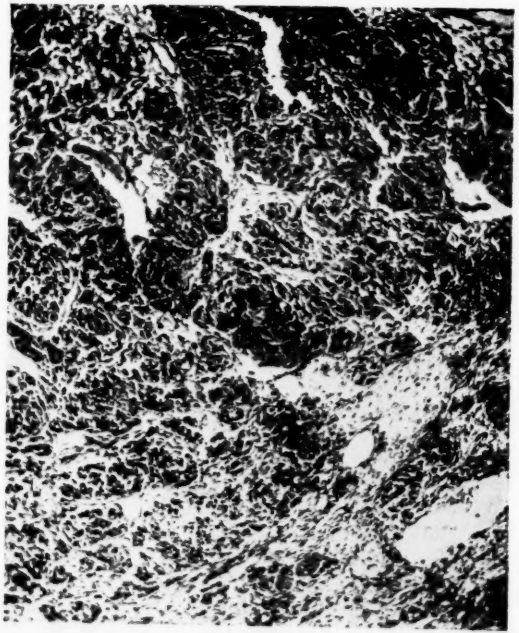
In the secondary tumour Jung found cells in trabeculae and having a plexiform arrangement. These cells also infiltrated the uterus. The illustrations of these cells show a marked resemblance to granulosa cells, although Jung believed them to be derived from a malignant endothelioma of the uterus. He considered the ovarian tumour to be a malignant embryoma. This theory, that he was dealing with two different tumours mixed up intimately together, is not now believed.

Cartilage in different stages of development was also present in a malignant teratoma reported by Emanuel.[3] The patient was a girl 15 years of age, and despite early operation the tumour recurred with generalized metastases. The appearance of the tumour agreed with Schiller's cases in showing the presence of cartilage and a sarcomata-like tissue, but fat, muscle and squamous epithelium were also present.

The history of the present case was as follows:

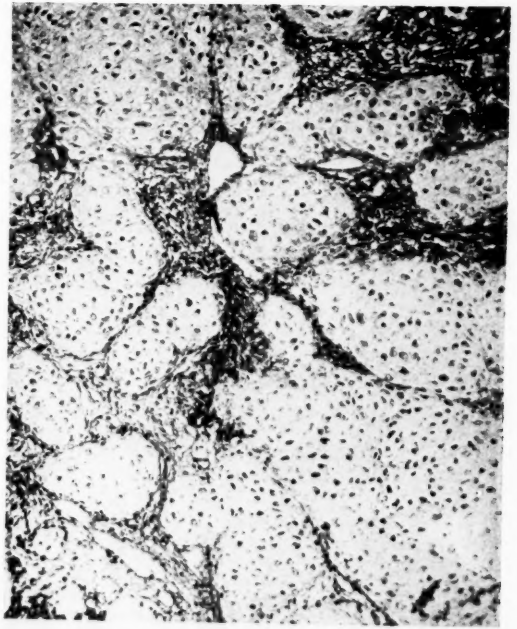
The patient was Mrs. H., aged 47, tripara, whose last child is 17 years of age. She had been bleeding irregularly for 3 months and thought she was simply having menopausal bleeding. She had seen her own medical man in the country, Dr. Chapman, who sent her to me immediately. She had no complaint other than the haemorrhage, was a strong-looking woman who was not anaemic and who had gained a little weight. There was a tumour palpable on bimanual examination and the cervix was markedly eroded. Laparotomy was advised.

When the abdomen was opened numerous adhesions presented themselves. These were separated and a tumour almost the size of a large grapefruit was apparent and involved the left Fallopian tube and ovary. It was densely adherent to the side wall of the pelvis and to the intestines, and it was necessary to isolate the left ureter as the tumour was in close proximity to it and to the large vessels. During its removal the tumour was ruptured and some cheesy material exuded. There was also a tubo-ovarian cyst on the right side. The removal of this presented some difficulty, but not as much as the tumour on the other side.



granulosa-like cells

FIG. 1.



cartilage

FIG. 2.

FIG. 3.

FIG. 4.

It was impossible to say if the tumours were endometriomatous or malignant, and total hysterectomy was decided on.

The operation was difficult because of the dense adherence of the bowel. Separation was accomplished by scissors and the uterus was removed. Drainage was carried on by the vagina and the abdomen. The convalescence was without incident. She was seen 6 weeks after the operation and the pelvis was clear.

In view of the following pathological report the question of deep X-ray therapy was considered and this was decided against.

Microscopically the tissue consists of a loose connective tissue which in most places contains masses of large, deeply staining cells having a close resemblance to granulosa cells (Fig. 1). The most conspicuous feature histologically are numerous cartilaginous islets scattered in an irregular manner throughout the section (Fig. 2). These cartilaginous islands stand out very clearly in sections stained with polychrome methylene blue, in which the cartilage appears crimson and the surrounding cells blue. In some places are tubules, such as are to be found in the *rete ovarii* and in arrhenoblastomata (Figs. 3 and 4). In a few areas are numerous dilated thin-walled blood spaces and some areas are necrotic and infiltrated with inflammatory cells.

In one of Schiller's cases there was much myxomatous tissue closely resembling true cartilage, all stages of development being found between a myxomatous stroma and true cartilage. He pointed out that the more the tissue is differentiated to form cartilage the more sharply bounded it is. In the case now described the cartilage is more mature than in any of Schiller's cases and the islets show a well-marked perichondral capsule in some places when the sections are stained with Van Gieson's stain.

As pointed out by Schiller, there is no analogy in granulosa cell tumours for the finding of cartilage. It has already been mentioned that while cartilage occurs very frequently in teratoid tumours, outside this group it is very rare. Halban[4] found a cartilaginous islet in an ape's ovary, but in that case there was no tumour formation. Jung's case and Emanuel's case have been dealt with. It would appear in this case, as in Schiller's, that the cartilage is differentiated out from the connective tissue and is not due to the development of cartilaginous 'rests'. In two of Schiller's cases there was no cartilage in the primary tumour, the cartilage only appearing in the recurrences. Schiller points out that there are two possible explanations of this heterologous formation of cartilage from mesenchyme. Firstly,

it might be caused mechanically by cells, which are destined to form cartilage, being carried into the tissue similarly to the way in which lipoblasts may get into the myometrium and cause a lipoma of the uterus at a later date. Secondly, and more probably, one may consider that the embryonal mesenchyme cells may have a latent prospective potency which in normal development never becomes activated. Fischel, whose theory of the development of the granulosa mostly from mesenchyme is now well known, has shown that the prospective potency of different tissues should not be underestimated and that mesoderm in particular possesses a much wider power of differentiation than is usually ascribed to it. Ebner[5] has said that mesoderm in every place has the potency of forming fibrous connective tissue, cartilage and bone, and has shown that in the healing of a fracture the cartilaginous callus is not invariably formed from pre-existing hyaline cartilage but is also formed from the periosteum.

If a section of the pelvic region of a 12 to 14 mm. embryo is examined one sees behind the hilum of the ovary the mesonephros with its small tubules, and behind this again the intervertebral cartilage. These tissues, all of mesodermal origin, come at an earlier stage of development from a type of cell common to all three tissues. The development of this type of tumour could be explained by believing that a cell having this three-fold prospective potency caused the growth of the tumour. Schiller's three cases were all malignant and we consider the tumour described by us malignant.

In selecting a name for these tumours Schiller considers that if one were to attempt to indicate the various characteristics of the tumour, the resulting name would be long-winded and clumsy. He suggests that the tumour should be described shortly as a "Desmoblastoma ovarii malignum" and we have adopted his nomenclature.

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Since this was written there has been a recurrence.

An unusual case of Breech Presentation of 8-months' Pregnancy complicated by a Tubo-ovarian Abscess.

BY

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MRS. S. K. had always been healthy. Her periods started at the age of 14 years, and lasted 7 to 8 days. The loss during the first 3 to 4 days was fairly painful. She last menstruated on October 6, 1937, and expected to be confined in July, 1938.

In March, 1938, the patient had severe pain in the right lower abdomen, which was relieved by heat and tincture of belladonna by mouth. Quite suddenly, on April 26, the patient had severe pains in the epigastrium. The pain was accompanied by a high rise of temperature, with rigors and occasional vomiting. She was kept constantly under morphia. The rigors occurred from time to time, and the abdomen became rigid. Peritonitis was suspected.

By May 3, 1938, the whole of the right abdomen was painful but the maximal amount of pain and rigidity was in the region of the gall bladder. Cholecystitis being suspected, salicylates of soda and Vichy water were prescribed. The pain markedly lessened, and the temperature, which had persisted between 103° and 104°F., fell to 100° to 101°F. Since the general condition of the patient did not improve, and the leucocyte count was very high, the patient was admitted to the Lahore Maternity Hospital. She was anaemic, and her tongue was furred.

On abdominal examination the whole of the right side was painful on pressure, the maximal intensity being a little above McBurney's point. There was rigidity in the iliac region. The fundus of the uterus reached to 3 fingers' breadth below the xiphisternum. The head of the foetus was palpable below the liver of the mother. The foetal heart was heard one finger-breadth above the navel on the right side.

On vaginal examination the cervix was soft, patulous, and admitted two fingers, and the feet of the foetus were felt in the external os.

TREATMENT.

The temperature for the last 2 days ranged between 100° and 101°F., and the pulse-rate between 116 and 126. The blood-count showed 20,000 leucocytes and 85 per cent polymorphs, which suggested pus in the abdomen. So it was thought advisable to rupture the membranes and deliver the child artificially.

First operation. On June 20 the leucocytic count was 25,000. A needle was passed into the swelling, and the pus was evacuated and a drainage tube was inserted in the region of McBurney's point. The pus was thick and not offensive. It contained staphylococci and streptococci. The temperature fell to 100°F., and the patient improved, but from June 5 the temperature again rose and the operation wound failed to drain. The hard swelling still persisted on the right side.

Second operation. On June 7, under avertin and nitrous oxide and oxygen anaesthesia, an opening was made over the swelling. A needle was passed through this opening and pus was evacuated. With the needle as a guide a counter opening was made in the incision of the first operation, three fingers' breadth to the left of the McBurney's point. The cavity was scraped gently, and the tissue and the pus were sent for examination to Dr. Vishwa Nath, assistant bacteriologist to the Government of the Punjab.

Pathological examination of the pus showed the presence of short chained streptococci, and the sections showed the presence of ovarian tissue, suppurative necrosis of the Fallopian tube, and a tubo-ovarian abscess.

After the second operation the wound dried fairly well. The fever subsided slowly, and the patient was discharged on August 16, 1938.

At the first examination the disease of the gall-bladder and liver was suspected, but rigors and very high rises in temperature and constant pain ruled these out. When the symptoms improved the examination revealed an appendicular abscess. The swelling was fairly high, and the pus was thick and had no smell. On the second operation both the right ovary and the right Fallopian tube were thought to be involved, and the pathological examination confirmed the diagnosis.

The Fallopian tube presumably got inflamed some time before conception. The inflammation remained latent till it started again in March, 1938, and subsided with ordinary treatment. The patient developed a tubo-ovarian abscess in May, 1938. The conception seems to have taken place through the patent left Fallopian tube.

We are indebted to Dr. Vishwa Nath for the pathological examination.

HOSPITAL REPORTS

ST. THOMAS'S HOSPITAL REPORTS. VOL. IV. SECOND SERIES, 1939. TOTAL NUMBER OF PAGES, 193.

This series of reports which has been received by the Journal contains many items which are not of interest to the gynaecologist and obstetrician. There are three sections which are, however, of considerable interest to us and they are:

1. "Investigation and Treatment of Vaginal Discharge," by Mr. A. J. Wrigley.
2. "Some points about Respiration, with special reference to Asphyxia Neonatorum and its Treatment," by Dr. M. D. Nosworthy.
3. Certain sections of the article on "The Male Sex Hormone," by Dr. J. S. Richardson.

The section concerned with the investigation and treatment of vaginal discharge is a clear and succinct account of this condition. Vaginal discharge in children, in the adult and in the post-menopausal phase of life are dealt with in chronological order and the reader is given a clear idea of the treatment which should be adopted in these various cases. It is particularly creditable to find that not only the names of drugs are given, as is so common in many articles, but it contains detailed instructions on the dosage and steps to be followed if the initial medication is unsuccessful. This article should be read by all students about to present themselves for the various examinations as it contains so much valuable knowledge in a relatively short amount of reading.

Dr. Nosworthy's contribution is very valuable in so far as it brings a knowledge of the respiratory mechanism to the fore. It is unfortunate in a way that the preliminary part of this article contains certain diagrams of Geudel's stimulus and threshold board. Unless one happens to be familiar with these they require considerable study to elucidate their meaning.

One of the first things which strikes one is the apparent lack of meaning of the solid inner lines in the absence of any explanation indicating whether the variable lengths signify the excursion of the threshold. It is believed, too, that the second series of figures would have conveyed their meaning so much more readily if they had been accompanied by some indication of the tidal air or graph of the respirations. Be that as it may, the part of the chapter dealing with the causes and treatment of asphyxia neonatorum is important to the obstetrician, and those specially interested in this subject should acquaint themselves with Dr. Nosworthy's correlation of the scientific and practical side of this subject.

Much of the material in this article appears to be based on the views of

Eastman published in the Bulletin of Johns Hopkins Hospital in 1932, and it might have looked better if this investigator's work had been referred to more specifically.

Dr. Richardson's contribution on the male sex hormone consists partly of the biochemistry of the hormone and related substances and partly of its practical use. Its use in the production of temporary sterility through suppression of ovulation and in cases of menopausal menorrhagia are discussed.

Other articles in this volume are written by other members of the hospital staff and deal with subjects in which they specialize. Although this publication is of high standard, it is noticed with regret that this type of hospital report gives the observer no idea of the real medical and surgical work conducted at the hospital.

Mortalities from the various diseases and the results of operations are no longer indicated as in the old form of the reports. This is an important fact to be borne in mind, particularly when it is remembered how interested the laity have become in recent years in comparing the results of general hospitals with those of the specialized hospitals. If the results, medical, surgical, and of the specialized departments, are as good as those of specialized hospitals, then it would appear wise to see that they are published even in an abbreviated form such as an appendix of the present volume. For instance, from the gynaecologist's and obstetrician's point of view, the results of the work of these departments at the hospital would have been of special interest to this Journal for comparison with other reports which are presented annually.

In other words the title of the volume, namely, *Hospital Reports*, is erroneous, since it does not contain any real mention of the hospital's work as such, but is a series of articles written by individuals on subjects in which they happen to be specially interested.

B. G.

WOMEN'S HOSPITAL, CROWN STREET, SYDNEY.

We are pleased to receive two publications from this hospital. They are the Forty-third Annual Report and the Medical and Clinical Report, July 1938 to June 1939.

The former, like so many other general reports, contains matter relating to the hospital administration, together with a long list of benefactors. In the course of the year 5,584 patients were treated in the wards and 3,520 babies were born. The hospital also provided teaching facilities for 113 students and 126 nurses.

The hospital is about to be considerably enlarged at a cost of about £140,000, this sum being expended on the provision of public, private and intermediate accommodation for maternity and gynaecological cases. The pathological and biochemical departments are also being enlarged.

The remainder of this publication does not contain anything further of medical interest.

The medical report is provided in a special publication mentioned below.

MEDICAL AND CLINICAL REPORT OF THE WOMEN'S HOSPITAL, SYDNEY.

In the course of the year the hospital treated 3,269 booked cases and 432 emergencies. The maternal deaths among the booked cases were six, giving a mortality rate of 1.835 per 1,000. There were 12 deaths in the emergencies. This gives a mortality rate of 23.936 per 1,000 for those delivered in the hospital and 53.57 per 1,000 for those admitted after delivery.

The rate for booked cases is very good, and we have commented on this when reviewing previous reports from this hospital.

We have only one criticism to offer, and that is that the degree of decimals to which the figures are given, although arithmetically correct, is of no scientific value past the first decimal point from the statistical point of view.

The report contains an interesting series of cases of breech presentation, the foetal mortality rate for which is 16.6 per cent. Nevertheless the mortality rate in cases of complicated breech presentation (e.g. placenta praevia, etc.) was 90.9 per cent. The morbidity rate for the obstetric department was 3.3 per cent.

In the course of the year Caesarean section was performed on 50 occasions; 35 of these were of the lower segment type.

In the section dealing with complications occurring during the puerperium one's attention is called to the fact that the most common complication other than major infections of the genital tract is mastitis, 115 cases, and breast abscess, 5 cases. In contrast to this only 1 case of cracked nipples is recorded. The incidence of mastitis appears to be particularly high in Sydney.

In the detail section dealing with the case records of the maternal deaths there is one interesting case in which the bacillus Welchii was cultured from the cervix. The records also contain an interesting table of the predominant organism in the birth canal in cases in which the temperature reached 101°F. or more following abortion. In 48 such cases the bacillus Welchii was the predominant organism in 28.

GYNAECOLOGICAL DEPARTMENT.

Records of the gynaecological department are not so thorough as the obstetric ones. In this connexion one may mention the 12 cases of carcinoma of the cervix which presented themselves at the hospital. It is impossible from this report to find the method of treatment. Under the heading of operations for diseases of the cervix there is no mention whatever of the treatment employed for these 12 women. Nevertheless in the list of deaths 1 case of carcinoma is present. It is stated that she had "hysterectomy performed," but this is not accompanied by any further details. Radium was applied 13 times, but no reason is given for the use of this substance. It is to be hoped that some at least of the cases of carcinoma of the cervix were given the benefit of radium.

Other than for minor criticisms of this kind the report from Sydney must be regarded as one of exceptionally high standard.

B. G.

BOOK REVIEWS

"Synopsis of Midwifery," by Jennings C. Litzenberg, M.D., F.A.C.S. London: Henry Kimpton. Pages: 394. Illustrations: 157. Price 21*s*.

The author has, in most sections, admirably achieved the brevity demanded by a synopsis and at the same time emphasized the really important in a lucid manner, which should appeal to the student bent on revision. This certainly applies to the reviewer recently called up from retirement to assist in teaching a group of undergraduates during the national crisis. Every word has been read but, of course, only a few of the sections can be referred to here, in a manner which is intended to be suggestive rather than critical.

With space too limited for discussion the author of a synopsis has to make a considered choice in many controversial matters. Dr. Litzenberg has shown wise judgment in his decisions. The chapters on Contracted Pelvis, with brief historical references, and on Ectopic Pregnancy, are particularly good. The importance of abdominal palpation of the foetus is fully recognized; credit is given to Pinard for his pioneer work, but, unfortunately, Leopold's procedure is described instead of the French obstetrician's much more rational and time-saving method. The author is, of course, not alone in this misjudgment. The management of normal labour, both as regards precise instructions and careful warnings, is admirably dealt with. It is surprising, however, that although "the most meticulous observation of all the rules of aseptic technique" is demanded, and rubber gloves are more than once specified, the use of face-masks is never mentioned. This is surely an oversight, or perhaps taken for granted. The only reference to shock is the statement, "Shock of unexplained origin is no longer a permissible explanation of sudden death in labour": a remark not in the least helpful to the junior student.

There are many unusually excellent illustrations, from several sources, great and most successful pains having been taken to select these "for their superior value for visual education." The matter is well classified in thirty-eight chapters and is most helpfully arranged under headings and sub-headings. The book ends with a really good index and the thoughtful provision of a few clear pages for the use of the keen student.

M. H. P.

"Public Health and Social Services," by D. H. Geffen, M.D., D.P.H., and L. Farrer Brown, B.Sc. (Econ.), Barrister-at-law. London: Edward Arnold and Co. 1940. Pages: 128. Price, 3*s*. 6*d*.

This is a good little book, written specially for pupil midwives and for midwives training for the midwife-teacher's certificate. In a series of twenty-

one chapters it covers the ground adequately, indeed almost too adequately at times. This is not intended as adverse criticism, for the book is always readable and, after all, midwives are years becoming a more highly trained body of professional workers. The chapters on public health administration and on the law relating to midwives are full of information, and other subjects dealt with include the control of disease, public medical services, social insurance, the care of children, and other matters on which some knowledge of the law is essential. An index would have added to the usefulness of the book, notwithstanding the generous table of contents provided.

Both authors possess great experience in their respective fields and they have compiled a handbook dealing with a very important part of the work of the modern midwife. No other book deals so satisfactorily with just those administrative matters a midwife ought to know. Practising midwives will find it a very helpful little work of reference and students an indispensable textbook.

Wilson Jameson.

"Midwifery for Nurses," by ALECK W. BOURNE, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G. London: J. and A. Churchill, Ltd. Price 6*s.* 6*d.*

THE second edition of this handbook on Midwifery, revised and brought up to date, will be welcomed by midwives and pupil-midwives. The author defines clearly the duties of midwives and the methods of treatment which they may carry out in emergency. The inclusion of a chapter dealing with Diet in Pregnancy is especially useful, while exercises for use in the puerperium are described and fully illustrated. It is rather surprising to find methods of artificial respiration described which are rarely taught at the present time. Icoral, a powerful cardiac stimulant is not mentioned, nor is any reference made to the sparklet apparatus or to the use of a nasal catheter when giving oxygen and carbon-dioxide to the infant. Varieties of puerperal sepsis are described, and the value of the sulphanilamides in the treatment of such cases. The use of sulphanilamide in the treatment of acute mastitis is not mentioned. This book should prove extremely useful for the midwife or pupil-midwife who wishes to refresh her memory on any point; it is concise, and contains valuable practical teaching. There are numerous excellent illustrations very well produced.

M. W. S.

Review of Current Literature.

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab.), F.R.C.S., F.R.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the "Journal of Obstetrics and Gynaecology of the British Empire" exchanges.

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world; owing to the war many journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received. At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology, and Biochemistry.

LIST OF ABSTRACTORS

J. LYLE CAMERON, F.R.C.S.; W. E. CROWTHER, M.B.; R. H. B. ADAMSON, M.D.; B. JEAFFRESON, F.R.C.S.; P. MALPAS, F.R.C.S.; T. N. A. JEFFCOATE, F.R.C.S.; MEAVE KENNY, F.R.C.S.; JANE H. FILSHILL.

British Medical Journal.

No. 4098, July 22nd, 1939.

*Phlegmonous gastritis in pregnancy. T. Barnett and D. P. Harris.

No. 4105, September 9th, 1939.

*Puerperal agranulocytosis after sulphanilamide. I. K. Gayris, V. B. Green-Armytage, and J. K. Baker.

Acute yellow atrophy of the liver. E. Townshend.

No. 4108, September 30th, 1939.

Oestrogenic hormone therapy. T. N. A. Jeffcoate.

No. 4110, October 14th, 1939.

Antirachitic value of human milk. J. C. Drummond, C. H. Gray, and N. E. G. Richardson.

No. 4112, October 28th, 1939.

Severe uterine inertia treated by cutting the cervix. J. V. O'Sullivan.

ACUTE PHLEGMONOUS GASTRITIS IN PREGNANCY.

This condition, otherwise known as suppurative linitis, is an extremely rare one, only about 200 cases having so far been reported, and none associated with pregnancy. In spite, or perhaps because of this, the subject is of some clinical importance to the obstetrician, for its physical manifestations may simulate those of peritonitis, etc., and unless thought of, the differential diagnosis may be difficult. In the present case the organism responsible was streptococcus, and the initial symptom was the persistent vomiting. This was apparently verified by the improvement resulting from routine treatment, but the condition recurred three days after discharge, accompanied this time by severe upper abdominal pain, generalized tenderness, and a rise of temperature. A diagnosis of concealed accidental haemorrhage was made, but operation was impossible on account of the patient's rapid deterioration, and she ultimately died with symptoms increasingly corroborative of the diagnosis. At post-mortem the uterus and its contents were normal, the peritoneum somewhat inflamed, and the stomach the site of the most extensive submucous gastritis. It is of additional interest to note that the patient had suffered for some time from a streptococcal otitis, for there would appear to be the most definite causative value in this fact.

PUERPERAL AGRANULOCYTOSIS FOLLOWING SULPHANILAMIDE TREATMENT.

Only 39 grains of sulphanilamide were used in this case, but the patient died 17 days after its commencement, with the symptoms typical of acute leucopenia. Considering the widespread employment of this group of drugs, such an eventuality is admittedly rare, though there is no doubt that many of the cases of so-called fatal *streptococcal septicaemia* are really of this nature. The chief point of interest in this case is, however, the small dose administered over a comparatively long period, and it provides additional urgency to the requirement of a complete blood-count, even in the absence of symptoms, after 25 mgms. have been given in any case.

Albert Davis.

The Canadian Medical Association Journal.

Vol. xlii, No. 1, January, 1940.

*Maternal mortality from the viewpoint of the obstetrician. P. A. McLeod.

Vol. xlii, No. 2, February, 1940.

*Dysmenorrhoea. E. V. Shute.

*Hyoscine in labour. W. J. Stevens.

Vol. xlii, No. 3, March, 1940.

*The management of labour in elderly primiparae. J. W. Duncan and W. E. Gibson.

*The diagnosis and treatment of endometriosis. George Hooper.

REVIEW OF CURRENT LITERATURE

Vol. xlii, No. 4, April, 1940.

*Dysmenorrhoea. Norman F. Miller, B.S., M.D.
*Some clinical lesions of the vulva. P. J. Kearns, M.D.

Maternal Mortality from the Viewpoint of the Obstetrician.

The maternal mortality rate for the province of Ontario has not been substantially reduced in the last 30 years. For women in the fertile period of life, child-bearing is the second greatest cause of death, and one mother dies for every 200 babies born alive. Many of these deaths are preventable. There are three factors controlling this death-rate, and these should be employed. They are antenatal care, hospital facilities and the attentions of a competent obstetrician.

Puerperal sepsis, which was formerly the chief cause of maternal deaths, has now taken second place, but its occurrence is still too frequent. Predisposing causes are toxaemia, haemorrhage, trauma, exhaustion and shock associated with labour. The most common source of infection is the secretion from the nose and throat of those in attendance. This source may be excluded if the attendants wear masks and when they are known to have a fresh cold or to harbour organisms they must be excluded from the labour room. The employment of an antiseptic, such as a halogen derivative of xylenol, is advocated by Colebrook, and immunizes the vulva to droplet infection by streptococci for several hours. The routine post-partum use of ergot is highly commendable. The complete isolation of infected cases and the employment of sulphanilamide will greatly lessen the death-rate.

The chief causes of death in Ontario since 1935 are the toxaemias of pregnancy. Routine antenatal care, which includes examinations of the urine, blood-pressure and body weight, will indicate the onset of these toxaemias. This necessitates very strict routine observation. The type of toxaemia should be recognized whenever possible. Minor types respond well to treatment and are not serious. Eclampsia and pre-eclampsia are the most serious conditions. They must be regarded as different stages of one condition. When pre-eclampsia fails to respond to treatment, which occasionally is the case, termination of pregnancy must be considered, as this will prevent eclampsia. The means of termination may present difficulties which only experience and good judgment can solve. The rule is to wait as long as possible until the child is viable, but it must be remembered that in severe toxaemias the child is liable to die *in utero*. Caesarean section may be employed in pronounced pre-eclampsia with rapid onset, but never when eclampsia has occurred.

The third greatest cause of maternal deaths is abortion. Post-abortum sepsis is the chief danger and is almost always due to interference. When the case is infected no intra-uterine manipulation should be made.

The fourth greatest cause is haemorrhage due to placenta praevia, premature separation of the placenta and the conditions which permit post-partum haemorrhage. Pre-natal care and treatment of toxaemias will prevent deaths due to premature separation of the placenta. Vaginal deliveries of

cases of placenta praevia must only be attempted under efficient hospital conditions, which include facilities for blood transfusion. In the slightly marginal type, mere rupture of the membranes will suffice, whereas Caesarean section is the treatment when the placenta is to any extent implanted on the dilating part of the lower uterine segment. Post-partum haemorrhage can be prevented. A close observation of the uterus, with judicious kneading when it relaxes, will control most haemorrhages. Occasionally when there is uncontrolled trickling of blood which would be likely to exsanguinate the patient, uterine packing with iodoform gauze is permissible when conducted in an aseptic manner. Embolism is a true accident, but it might possibly occur less frequently if delivery were effected with little trauma and loss of blood, and if encouragement were given to move freely in the puerperium.

Caesarean section is a life-saving operation, but the cases which are to be treated in this way must be chosen carefully. Adequate antenatal care will anticipate most of the difficulties which are to be encountered and means for dealing with them may be chosen with deliberation.

The author expresses a plea for more extensive training in obstetrics for undergraduates.

DYSMENORRHOEA.

The author discusses 130 cases, ranging in age from 14 to 48 years, 86 being married. These cases were classified as follows:

(*a*) Endocrine dysmenorrhoea, excess or deficiency of blood oestrogen—35 patients.

(*b*) Inflammatory dysmenorrhoea, tubal inflammation or parametrial cellulitis—6 patients.

(*c*) Mechanical dysmenorrhoea, fibromyomata uteri, endometriosis and ovarian cysts—16 patients.

(*d*) Mixed types—51 cases.

(*e*) Unclassified, membranous dysmenorrhoea—24 cases.

The author admits that there are many puzzling features about menstrual pain. In many the pain was colicky in character, but by the majority it was described as a constant ache. Endocrine derangements seem to be the most fertile cause of menstrual pain.

Treatment. Thyroid extract was used extensively and up to the limit of tolerance. It was found, however, that this method of therapy had to be continued almost indefinitely.

Progynon B (Schering) and gonadogen (Upjohn Co.) were used extensively. The latter appeared to be more effective in intermenstrual pain. Prolan preparations appear to be more effective and rapid in action. Progesterone and testosterone propionate and wheat-germ oil were also employed. The author found short-wave diathermy much more beneficial than hot douching. Endometriosis was treated by destroying the ovaries or treating them with deep X-rays.

A full bibliography is appended.

REVIEW OF CURRENT LITERATURE

Hyoscine in Labour.

Hyoscine is an analgesic and semi-hypnotic agent and has been used for many years in obstetrics. It is a strong cerebral sedative with amnesic properties. Occasionally it causes a form of delirium. It does not affect the respiratory system of the baby. The initial dose is $\frac{1}{100}$ gr., given when the os is dilated to the size of two fingers and pains occur every five minutes. Successive doses should be $\frac{1}{100}$ gr. till four doses in all are given. Ether by inhalation may be given to quieten the patient if she becomes restless, or just at the birth. The author has used hyoscine in this way in over 200 cases, and the results for both mother and child are very good. The mother appears to have no memory of the labour.

The Management of Labour in Elderly Primiparae.

Numerous accounts are given of the rare cases of elderly primiparae having swift, easy and uncomplicated labours. These cases, though outstanding, are definitely in the minority, and for the elderly primipara and her child, labour has many dangers, and although the death of a new-born baby is a tragedy, the birth of a mentally injured child is a calamity. The aged primipara has few chances of conceiving again.

A study is made of 1,179 women of 30 years of age and over. These are divided into three groups, those between 30 and 35, those between 35 and 40, and those of 40 and over. From these tables it was shown that pre-eclampsia and eclampsia were much more frequent in the case of older women, the incidence of pre-eclampsia being four times and that of eclampsia twice as great as in younger patients. The occurrence of these complications was shown in the tables to be highest between the ages of 35 and 40.

Pelvimetry and vaginal examination revealed a high frequency of pelvic deformity, especially that conforming to the male type. As the result of these deformities 15 per cent of women between the ages of 35 and 40 were delivered by Caesarean section. In the group of women over 40, 36 per cent were so delivered, and in the group between 30 and 35, operation was performed in 5.9 per cent of cases.

When elderly women have been married a long time before conception occurs, and when there has been irregularity of menstruation, inertia in labour must be anticipated, and when the first stage of labour is attended by feeble contractions, Caesarean section should be performed without delay.

When there is any degree of disproportion, a trial of labour is only justified in women under 35. After this age every case should be delivered by operation. In all patients over the age of 35, when there is a rigid, long cervix, it is much safer to deliver by abdominal section. In all women of 40 years of age and over, unless the head is very deep in the pelvis and the lower uterine segment is very thin, delivery through the pelvis is unjustifiable.

The management of labour and antenatal care should begin as early and be as thorough as possible, and a definite plan of action should be instituted at once.

From the study of these groups the author is of the opinion that, as

regards obstetrical risks, in women between 30 and 35 years of age these are poor, between 35 and 40 bad, and over 40 very bad indeed.

Diagnosis and Treatment of Endometriosis.

Endometriosis was an obscure subject until 1921 when Sampson reported 23 cases. The condition was described by von Rokitansky in 1860, but was called adenomyoma, and von Recklinghausen in 1896 described "tumours arising from the Wolffian duct." Russell in 1899 wrote of the occurrence of endometrial tissue in the ovary, and later Cullen wrote extensively about adenomyoma, but did not seem to define clearly the relation between this condition and endometriosis. Meigs in 1938 advanced the theory that endometriosis resulted in some way from the practice of contraception.

At the present moment many are asking if the indiscriminate employment of oestrogenic hormones may be causing endometriosis. It has been reported that the condition has been found in 35 per cent of all cases of abdominal gynaecological operations, but the earlier clinicians did not seem to note this frequent incidence. They were keen observers and scrupulous recorders of their findings and could scarcely have missed the disease had it been present.

Attempts were made by the author some years ago, under great difficulties, to determine by endometrial biopsies at different stages of the menstrual cycle and by estimations of prolan A and oestrin in the blood, whether or not there was relation between the occurrence of endometriosis and increased oestrin production. This seemed to be the case.

Symptoms of endometriosis arise during that period of life when menstruation occurs, and they are much more severe in younger patients. They have not been seen before puberty, and adenomyoma of the uterus has been noted when the uterus was removed in women of 70. These elderly women had had no previous symptoms and had given birth to numerous children, but this is unusual with this growth present.

The most common symptoms are acquired dysmenorrhoea which occurs throughout the period; backache, intermenstrual pain, irregular menstruation, menorrhagia, leucorrhoea, rectal and vesical haemorrhage, intestinal obstruction and nervous instability. Only occasionally are all the symptoms present in one patient.

Endometriosis does not appear to involve any of the structures above the umbilicus but all the organs below and including it. Sampson's theory is that there is a retrograde flow of portions of the endometrium which pass along the Fallopian tubes, become implanted in the ovary and other pelvic structures and invade these; they undergo the same phases in their new situations as the endometrium in the uterus. The symptoms are caused by active stimulation of the new endometrial tissue by oestrin; the growth in many ways simulates carcinoma. It invades the ovary, causing chocolate cysts, or it may invade the bowel, causing obstruction and massive adhesions of bowel and other pelvic organs. After an abdominal section it may be difficult to differentiate such a mass from carcinomatous growth, but the presence of one or more blue-domed cysts will make the diagnosis clear.

There is usually irregular and profuse menstruation, progressive in type and not responding to endocrine medication. Rectal bleeding may occur, but is periodic and associated with menstruation. Haematuria may take place but is also periodic, and blue-domed cysts are visible on cystoscopic examination. There may be swellings in the groin or growth in the round ligament which are always tender and larger during menstruation. Chronic appendicitis may be simulated and when such a diagnosis is made, the pelvis should be carefully explored to determine whether or not any endometrial growth is present. The diagnosis cannot always be made with certainty, and should be provisional in almost every case.

In the early cases there is usually pain associated with menstruation, and in the advanced cases the uterus may be pulled backwards and partially fixed, and there will probably be pebbly thickening of the recto-vaginal septum. In the author's opinion a thickened recto-vaginal septum with partial obliteration of the pouch of Douglas is a diagnostic sign. The recto-vaginal examination gives more information than a vaginal examination only. Swellings are usually felt in the region of the ovaries, but are seldom larger than a small orange. If they are larger one must suspect a dermoid cyst. If intestinal obstruction is associated with the findings just cited one must suspect endometriosis as the cause.

The disease can usually be cured, but the price of cure is too high. If the patient be deprived of oestrin by operation or other means the growth will retrogress, but adhesions will remain. When the disease is widespread and has extensively invaded structures, radical treatment may be necessary, especially if the patient is near the menopause. Conservative treatment should, whenever possible, be practised, especially in the young, symptoms being treated as they arise. When operation becomes necessary every effort should be made to conserve part of at least one ovary as this will preserve its function and child-bearing may still be possible. The patient should, however, be apprised of the possibility of conservative methods having to be followed at a later date by some more radical procedure. Treatment with radium and X-rays may be followed by too extensive destruction of the ovarian tissues, and even sloughing of other tissues, and yet must always leave the mechanical adhesions untreated. After radical operation, oestrogenic hormones should not be given as they will cause a recurrence of the symptoms.

A short bibliography is appended.

DYSMENORRHOEA.

Recently there has been a great increase in the knowledge of the causes of menstrual pain, but there has not been a proportional effectiveness in curing the condition. Dysmenorrhoea is a major problem because it is so often an incapacitating illness. Approximately 45 per cent of women suffer some discomfort during menstruation, about 15 per cent are seriously inconvenienced.

Classification is difficult and not very satisfactory, but long usage justifies the grouping into primary or essential types, in which the symptoms begin

early in menstrual life, and secondary or acquired types when the pain arises in later years. Primary dysmenorrhoea is characterized by crampy pain, while the secondary type is characterized by a steady ache. Frequently, however, both types occur in the same patient. There are often, in addition, constitutional symptoms such as nausea and vomiting.

Treatment must be founded on a thorough understanding of the anatomy and physiology of menstruation. It is well known that there is a relation between menstrual disorders and the emotions, exemplified in blushing, nervous indigestion, sweating, tachycardia and urinary urgency, but it is not known whether these are due to nerve impulses or to internal gland derangements. Menstruation may be disturbed by emotional upset or by inflammatory or degenerative changes of the ganglion cells of the uterine nerves. Care should be taken to determine as far as possible psychogenic factors when investigating cases.

The vast venous supply of the pelvic organs affords a mechanical condition which, if these veins were greatly engorged with blood, would cause very greatly increased menstrual pain.

There has been much discussion recently of endocrine action on the uterus. Oestrin appears to stimulate and progestin to inhibit the symptoms. The use of corpus luteum hormone clinically has not been highly satisfactory. It would appear, too, that hypoplasia of the uterus was a factor of some importance. Dysmenorrhoea does not appear to be associated with anovular bleeding. The exact mechanism by which pain is produced is unknown.

Treatment of the pain has two objects, first, the relief of the pain, and secondly, the cure of the underlying cause. Occasionally the relief of pain is easily obtained, but cure of the underlying cause is extremely difficult. Peace of mind is an important factor, and the removal of emotional disturbance such as might be engendered by anxiety may go far to remedy the difficulty. The drugs which have proved to be valuable are atropin, phenacetin, and aspirin, together with caffeine, strontium bromide, and also codeine. These drugs may be employed singly or in groups and are often highly effective. In primary dysmenorrhoea, endocrine therapy may be useful, and oestrin may hasten the development of an immature uterus. Secondary dysmenorrhoea is treated on similar lines, the first object of treatment being to correct underlying causes such as displacements and inflammations, and the removal of growths. Allergic cases of dysmenorrhoea must be kept in mind as must also neuritic (not neurotic). Pre-sacral neurectomy for intractable cases is occasionally necessary, but the need for it is not great.

A short bibliography is appended and several excellent diagrams are included in the text.

SOME CLINICAL LESIONS OF THE VULVA.

Malformations of the genitalia, whereby the condition of pseudo-hermaphroditism is produced, are not uncommon; yet true hermaphroditism, in which male and female gonads together with functioning Wolffian and

Müllerian ducts are present, is extremely rare. The latter, however, appears really to have happened and to have been associated in a recorded case with autogenous fertilization.

Abnormal growth of the mesoderm between the ectoderm and entoderm of the cloacal membrane may produce varying degrees of imperforate hymen and closed proctodaeum. Excessive growths of mesoderm may, in later life, produce enormous labia minora. Rarer abnormalities are haemangiomata of the vulva; yet still rarer occurrences are cystic inclusions of the Wolffian remnants between the hymen and the clitoris, and there may be distention of the canal of Nück.

Varicosities of the vulva usually arise during pregnancy, and if subjected to trauma be the source of extensive extravasation of blood. Operation may be necessary to remove enlarged varicose veins or to evacuate a haematocoele —in the latter case to prevent infection and necrosis.

Acute vulvo-vaginitis may be due to mechanical irritation or to gonorrhoeal discharge. Vulvo-vaginitis in children is usually gonorrhoeal, but may occur during scarlet fever, throat infections, or be diphtheritic. Chronic vulvitis may follow septic uterine discharge. Erysipelas following child-birth, one of the cases being fatal, has been seen on two occasions by the author.

When dermatitis of the vulva occurs, one must always suspect diabetes and other constitutional disorders of being possible causes.

Acute ulceration of the vulva, most commonly seen in negresses and women who have had syphilis, may be associated with extensive fistula formation. The condition is not affected by anti-syphilitic treatment and heals only slowly under hygienic measures. The author cites a case of extensive ulceration of the vulva which defied all means of treatment until large doses of vitamins A and B were given, when it healed rapidly.

Ducrey's chancroid lesions of the vulva have been seen in the author's clinic and an illustrative case is cited.

Tuberculous lesions of the vulva, most commonly seen as secondary, have been noted as a primary condition among the author's cases. There are two types of lesion, one ulcerative, and the other hypertrophic, producing a polypoid growth undistinguishable from a syphilitic lesion or an early carcinoma.

Syphilis of the vulva may occur as a hard chancre or as primary or secondary papules, and either may occur on the vestibule, commissures or the nymphae. A case is cited of tertiary indurated swelling and ulceration of the labia and posterior commissure.

Diabetic granulomatous ulceration of the vulva has been seen. Diabetic irritation led to scratching which was followed by an infection causing extensive lesions. The condition improved only when rigorous diabetic treatment was instituted and dressings of insulin were employed locally.

Benign tumours of the vulva were exemplified as ordinary warts. In no case was carcinoma known to arise in these growths. Fibromyomata and lipomata were seen, both growing to the size of a child's head. Other growths were angiomata, chondromata, and neuromata, all very rare. Condylomata were not infrequently seen in women who had borne children. These were

treated by the local application of the cautery and by careful hygienic measures.

Cystic tumours of the vulva were seen as dilatation of Bartholin's gland and duct.

Endometriomata of the vulva, formerly called sarcoma, were characterized by the presence of raised thickened areas on the vulva and vagina. They are very slow growths. This growth differs from endometriosis in being composed of an organized strauma devoid of glands. The growth extends along blood-vessels and lymphatics in parallel lines. Treatment with deep X-rays appeared to be satisfactory.

Degenerative diseases of the vulva, such as senile atrophy, were frequently noted. The labia became atrophied and shrunken, and the vagina gaping, permitting the ingress of organisms which led to senile vaginitis. The condition was treated satisfactorily with lactic acid and oestrogenic medication.

Kraurosis vulvae was occasionally observed as a diffuse hypertrophy and overgrowth of the papillary bodies of the corium, leading to a leathery, dry condition of the skin. There was a diffuse thickening of the epithelial layers due to infiltration with lymphocytes and fibroblasts. The treatment prescribed was oestrogenic and high vitamin medication, and when this failed, excision of the vulva to include all the affected part.

Malignant growths of the vulva. Sarcoma of the vulva is extremely rare; melanotic growths are classed as carcinomatous. A case was reported of a sarcomatous nodule in the vulva secondary to a massive primary growth in the pelvis.

Adeno-carcinoma occurred in Bartholin's gland. Other carcinomata arise on the surface of the vulva, especially following leukoplakic vulvitis. About 25 per cent of all vulval carcinomata begin in association with leukoplakia.

A brief report is given of 13 cases of malignant growths of the vulva seen over a period of three years. They were treated chiefly by radium and electro-cautery. Of these four, or 30.7 per cent, were alive five years later.

J. Lyle Cameron.

American Journal of Obstetrics and Gynecology.

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The hippuric acid excretion test in pregnancy. A. Hirsheimer.

*Morbidity following radical operations for pelvic inflammatory disease. Della G. Drips and Lois A. Day.

The Manchester (parametrial fixation) operation for cure of prolapse and cystocele. Michael L. Leventhal and Louis D. Boshes.

*The influence of the hormonal activity of the ovaries upon the character of tubal contractions as determined by uterine insufflation. I. C. Rubin.

*Rôle of the uterus in the production of manometric fluctuations during

utero-tubal insufflation (Rubin's test). S. Wimpfheimer and Morris Feresten.

Pregnancy with leucaemia. R. M. Grier and H. A. Richter.

*Granulosa cell tumours. Malcolm B. Dockerty and William C. MacCarty.

A fifteen-year study of Caesarean section in the Woman's Hospital in the State of New York. Ralph L. Barrett.

Retrodisplacements of the post-partum uterus. Sanford H. Moses.

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The effect of progestin upon the anterior pituitary. A. W. Makepeace.

Food habits of mothers of congenitally malformed children. Douglas P. Murphy and Anna De P. Bowes.

Ante-partum rupture of the uterine scar following low flap Caesarean section. J. R. Gepfert.

Puerperal sterilization. Fred L. Adair and Ira Brown.

Granuloma venereum of cervix uteri. Edgar R. Pund, Georgia B. Huie, and V. A. Gotcher.

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Precocious puberty due to an ovarian cyst in a five-year-old girl. William F. Mengert.

Rupture of urinary bladder complicating early pregnancy. Louis Langman.

Oestrogenic hormone in the urine and tumour of a patient with a granulosa cell tumour of the ovary. Allan Palmer.

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Relaxation of the pelvic ligaments in pregnant monkeys. Carl G. Hartman and William L. Straus, Jr.

Eutocia complicated by lymphopathia venerea, perirectoanal mass, and rectal stricture. Harley E. Anderson.

Endometriosis of the umbilicus. William Berman.

Intraligamentous, parovarian cyst. Manly E. Hutchinson.

A new obstetric phantom. Walter B. Mount.

A simple, safe and economical cord tie. H. M. Kanner.

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*Studies on the endometrium in association with the normal menstrual cycle, with ovarian dysfunctions and cancer of the uterus. Wallace E. Herrell.

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*Behaviour of the basal metabolism in the course of developing toxaemia of pregnancy: correlation with cholesterol, placental infarcts and retinal examination. E. D. Colvin and R. A. Bartholomew.

Clinical syndromes referable to failure of ovulation. Emil Novak.

The aetiology of occiput presentations. L. A. Calkins.
The increased incidence of foetal abnormalities in cases of placenta praevia. J. P. Greenhill.
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*Prevention and treatment of post-operative thrombo-phlebitis. N. W. Barker and V. S. Counseller.
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Benign tumours of the cervical stump following supravaginal hysterectomy. Mortimer N. Hyams.
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*The effect of oestrogenic hormone on the H-ion concentration and the bacterial content of the human vagina, with special reference to the Döderlein bacillus. Louis Weinstein and Joseph H. Howard.
Brenner tumours of the ovary. M. B. Dockerty and W. C. MacCarty.
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*Do eclampsia and pre-eclampsia cause permanent vascular renal pathology? William J. Dieckmann and Ira Brown.
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The clinical significance of endometriosis. Virgil S. Counseller.
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The clinical significance of appendices epiploicae. Howard C. Walser.
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Daily gonadotropic hormone tests during fifty complete menstrual cycles. Fred E. D'Amour, Dorothy Funk, and Helen Liverman.
*The aetiology and treatment of endocervicitis. Anthony Wollner.
*Hormone factors in the toxaemias of pregnancy. Howard C. Taylor and Eugene N. Scadron.
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Foetal and neonatal disease and death. Fred L. Adair and Edith L. Potter.
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The therapeutic value of low-dosage irradiation of the pituitary gland and ovaries in functional menstrual disorders and sterility. Charles Mazer and George Baer.
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Massive intraperitoneal haemorrhage resulting from rupture of a superficial vein of a uterine fibromyoma. Anthony L. Shelfo.
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Cervical dystocia due to scars from deep cauterization. Harry James Jordan.

An instrument for the safe drainage of ovarian cysts. Adrian W. Voegelin.
Automatic transuterine tubal insufflator. Oscar H. Bloom.
Study of maternal deaths in Chicago. Fred L. Adair, Augusta Webster, and Luella Nadelhoffer.
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Selected abstracts—Analgesia and anaesthesia in labour.

MORBIDITY FOLLOWING RADICAL OPERATIONS FOR PELVIC INFLAMMATORY DISEASE.

Although it is the policy of the gynaecologists at the Mayo Clinic to treat acute pelvic inflammatory disease medically when there is no doubt about the diagnosis, it was necessary to operate upon 300 cases between 1925 and 1935. Of these, 183 cases were followed up to August, 1939, and in these the indications for operation had been the inability to control or reduce the pelvic mass by medical means, while in a few it had been impossible to differentiate from acute appendicitis. The authors point out that this rather short series seems to reveal that so-called plastic operations on the pelvic organs are useless. They think that the morbidity after conservative operations may be reduced by medical treatment but they consider that it is best to remove the uterus if any ovarian tissue is left behind unless this is perfectly normal. Pregnancy was unusual and it occurred only in cases in which one side alone was affected.

THE INFLUENCE OF HORMONE ACTIVITY OF THE OVARIES UPON THE CHARACTER OF TUBAL CONTRACTIONS AS DETERMINED BY UTERINE INSUFFLATION.

In a series of 513 patients the tone and the activity of the Fallopian tubes and uterus were investigated by utero-tubal insufflation and the findings were analysed in relation to the type of menstrual cycle presented by each patient. In patients with normal menstrual cycles contraction and relaxation occurred about three times per minute in the anovular phase, while about the period of ovulation the tone increased and the rate of contraction became about 8 per minute. In cases with a long menstrual cycle and with amenorrhoea, the tone and the frequency of contractions both diminished, being least in the amenorrhoea of the menopause. In patients with prolonged menstruation the utero-tubal tone and the contraction rate was less than normal but greater than in the above group. The author concluded that there was a relation between the tubal contractions and the hormonal activity of the ovary and, as additional support for this idea, he demonstrated the dynamic effect of progynon in a case of prolonged secondary amenorrhoea.

ROLE OF THE UTERUS IN THE PRODUCTION OF MANOMETRIC FLUCTUATIONS DURING UTERO-TUBAL INSUFFLATION (RUBIN'S TEST).

Fluctuations of pressure during insufflation of the uterus and Fallopian tubes of living rabbits only occurred if the tubes were patent. During in-

sufflation the uterus distended and rhythmic movements in it disappeared, while movements in the tube were unaltered. By shortening the tube from the ampullary end, it was shown that almost all the power of contraction was located in the muscular isthmus. The authors concluded that the uterine muscle had very little influence on the kymographic record of pressure changes during utero-tubal insufflation.

Granulosa Cell Tumours.

Because of work already published the conception that granulosa cell tumours arise from granular cell rests can be held no longer. In women 60 per cent occur after the menopause, when they give rise to pseudo-menstrual bleeding; 30 per cent are discovered during sexual maturity when they may cause amenorrhoea or menorrhagia; the remaining 10 per cent are seen in children and cause precocious sexual development. In all cases a large amount of oestrin can be found in the tissues, blood and urine. From a study of 30 cases of granulosa cell tumours at the Mayo Clinic, the authors found menstrual changes in 27; the neoplasms were unilateral in every case. In 15 out of 17 uteri which were available for examination, the endometrium showed polypoid-cystic changes, and it is suggested that such a finding associated with post-menopausal bleeding demands laparotomy.

Two patients died from operation, 2 could not be traced, but of the rest only one had a recurrence. It is therefore suggested that in young patients the removal of the tumour alone, with perhaps post-operative medication, is adequate treatment, whereas a more complete operation should be performed in older women.

On histological evidence it is thought that the tumours arise from granulosa cell rests or degenerating Graafian follicles.

Studies on the Endometrium in Association with the Normal Menstrual Cycle, with Ovarian Dysfunctions and Cancer of the Uterus.

The endometrium reflects changes in ovarian hormone secretion, whether these be primary or dependent on other endocrine disturbances. If the balance between the follicular and corpus luteal hormone is upset there are changes in the endometrial cycle. These may be represented by a "persistent phase" which shows histologically the accepted features of the phase at which the cycle has stopped, often together with cyst formation. Micro-photographs demonstrate these features. In cases of a persistent proliferative phase the tendency is to bleeding rather than sterility, while in cases of persistent differentiative phases the greater tendency is to sterility. In 50 cases of carcinoma of the body of the uterus the endometrium was almost always in the proliferative phase. The ovaries in such cases were usually cystic and may be the origin of the oestrin which was found in the urine in 95 per cent of the cases examined. So far as the author could determine,

carcinoma of the body of the uterus has never been seen in a patient previously castrated.

Behaviour of the Basal Metabolism in the Course of Developing Toxaemia of Pregnancy: Correlation with Cholesterol, Placental Infarcts and Retinal Examination.

A series of 62 adolescent coloured primigravidae were examined. The basal metabolic rate and blood cholesterol content were estimated, the retina was inspected for changes and placentae were examined histologically. In this series, 38 per cent showed signs of toxaemia as against only 4 per cent in 100 primigravidae, aged 25 to 30, in the author's private practice, and in these latter cases the toxaemia was generally less severe. The incidence of toxaemia was higher in cases of hypothyroidism and these were associated with a high blood cholesterol content. The more severe the toxaemia the more acute were the placental infarcts and the arterial spasm in the retina was more pronounced. The authors suggest that cholesterol vascular changes in the placental vessels predispose to infarction, with which is associated the toxaemia, and they suggest that the administration of thyroid extract may therefore be an effective measure in preventing toxaemia.

Prevention and Treatment of Post-operative Thrombo-phlebitis.

Lesions of the intima, blood stasis and an increased coagulability of the blood play a part in post-operative thrombo-phlebitis. The incidence is highest in pelvic operations and in patients with varicose veins, but no satisfactory prophylactic measures are yet available. Thrombosis of the short saphenous vein often passes unnoticed and is rarely serious. In cases of thrombosis of the big veins, the risk of embolus is greatest at the time of the formation of the thrombus and rapidly diminishes. The treatment adopted is to elevate the limb to 30°, to give opiates for pain and to apply hot packs continuously. The patient is allowed out of bed when the pain and the swelling below the knee have gone and the temperature has been normal for three days, providing that an elastic support is worn below the knee. In 80 per cent of cases the patients were up within 16 days.

The Effect of Oestrogenic Hormone on the H-ion Concentration and the Bacterial Content of the Human Vagina, with Special Reference to the Doderlein Bacillus.

The vaginal secretion was examined in 9 cases of post-climacteric patients in whom there was no evidence of organic disease. The authors conclude that if the *p*H is near the neutral point the acidity can be increased by administering oestrogenic hormone and that this change can occur without the presence of Döderlein's bacillus. Moreover, they failed to find a definite relation between the acidity and the presence of Döderlein's bacillus and they suggest that an enzyme may be present which is responsible, in part at least, for the breakdown of glycogen.

COLLAPSE THERAPY FOR TUBERCULOSIS IN PREGNANCY.

There is still divided opinion on what is best to be done when pregnancy is complicating a case of active pulmonary tuberculosis. Many authors hold that tuberculosis is so frequently made worse by pregnancy as to offer an absolute indication for therapeutic abortion. On the other hand, others state that child-bearing has a negligible effect on the lung condition. Probably an intermediate position should be taken, and such factors as duration of pregnancy, parity, and type of tuberculous lesion should be taken into account.

In this series, 109 tuberculous women were delivered and subsequently treated in a period of 7 years, and they were studied in order to see the effects of the pregnancy on the lung condition. Fifty-four of these patients were in hospital for not less than 2 months before delivery and they received collapse therapy during that time; 11 were under observation for the two months but either refused treatment or it was considered inadvisable; and the remaining 44 patients received little or no treatment for their tuberculosis.

All cases were transferred to the tuberculosis department 7 to 10 days after delivery and all received treatment. Thus in this series it is possible to compare three groups of patients, all of whom received the same care after delivery but different treatment for the tuberculosis before delivery. Collapse therapy was performed mainly in those cases of moderate lung involvement; the next largest number of cases occurred in the group of advanced lesions; while the group of minimal lesions contained the fewest cases of collapse therapy.

The maternal mortality was 6 in 54 cases treated with antenatal collapse therapy; 1 in 11 with hospital treatment without collapse, and 16 in 44 cases with little or no prenatal treatment. All deaths occurred after delivery and they were due to the tuberculosis. The 54 cases with collapse treatment did comparatively well. Thirty-eight of these were definitely improved in spite of the pregnancy, and in 6 cases the disease was arrested. The moderately active lesion, whether in an advanced state or not, seemed to react best to this form of treatment, and the final prognosis was apparently better in multiparae than in the primigravidae.

The authors are of the opinion that collapse therapy should be seriously considered in all cases of tuberculosis of the lung complicated by pregnancy. The method of collapse should be governed by the pulmonary lesion rather than any consideration of the stage of the pregnancy. Therapeutic abortion should be performed in some cases in the early stage of pregnancy, especially if the lesion is early and active and in a primigravida.

DO ECLAMPSIA AND PRE-ECLAMPSIA CAUSE PERMANENT VASCULAR RENAL PATHOLOGY?

Opinions on this very important question vary considerably. No text-book states specifically what percentage of eclamptic or pre-eclamptic patients are likely to have permanent damage, a recurrence of the toxaemia, a

subsequent normal pregnancy, or will abort or have a stillborn foetus. The authors first stress the importance of a recognized classification of albuminuria occurring with pregnancy and they recommend that all cases should be divided into eclampsia, pre-eclampsia, essential hypertension, vascular renal disease, and acute or chronic glomerulo-nephritis; and they state that they can demonstrate distinct differences between these groups.

They have followed up 56 eclamptic patients during the past 7 years; 8 of these had a subsequent pregnancy under their care and 2 were pregnant at the time of their report. Of these, only 1 had a raised blood-pressure. Two hundred and twenty-five patients with non-convulsive toxaemia had two or four pregnancies in their clinic; of these, 27 per cent had a normal subsequent pregnancy and 73 per cent had a repetition of the toxaemia. Over 40 per cent of the patients had vascular-renal disease, as evidenced by a persisting hypertension, and renal impairment occurred in 2 per cent. Chronic glomerulo-nephritis was present in 0.5 per cent. The authors are of the opinion that true eclampsia and pre-eclampsia do not cause permanent vascular or renal damage and that, where such damage occurs, either the condition was not eclampsia or pre-eclampsia or these diseases were superimposed on a patient with a predisposition to hypertensive arterial disease.

URETERAL INJURIES IN GYNAECOLOGIC SURGERY.

Injury to the ureter occurs at intervals in pelvic surgery and is always a very important complication. The authors state that it has been estimated that it occurs in 1 to 3 per cent of all pelvic operations, and they believe that many cases must occur unrecognized to account for this high figure. To provide against this accident, it is necessary for every surgeon to realize that the ureter is 1.5 cm. from the uterus at the internal os and 1.0 cm. from the cervix at the vaginal reflection and that this relation is profoundly modified by extensive pelvic pathology. Inclusion of the pubo-cervical fascia in the lower clamps during the performance of total hysterectomy diminishes the possibility of injury to the ureter. When there is troublesome bleeding during the enucleation of an intra-ligamentous fibroid, the authors advocate packing rather than trying to seize the bleeding points.

The authors quote a series of 13 cases of ureteral injury which occurred during a period of 15 years. The larger proportion of these cases occurred after 1930, when the staff began to perform total hysterectomy more often, but one is included where supra-vaginal hysterectomy was performed at another hospital. In 2 of these 14 cases the injury was bilateral. Six cases had total hysterectomy performed, and in 1 of these the enucleation of an intra-ligamentous cyst as well; 4 had a colporrhaphy operation for cystocele; 2 had had subtotal hysterectomy; 1 had an enucleation of an intra-ligamentous cyst following a previous subtotal hysterectomy; and 1 had a Wertheim's hysterectomy. The authors stress the importance of early recognition of bilateral injury and advise that the bladder is completely emptied at the end of any operation in order to be sure that the two ureters have sustained no injury. If no urine is obtained, treatment must be

instituted at once. Ureteral catheterization will decide whether the anuria is due to unilateral occlusion with reflex suppression from the other kidney or not. Intravenous urography is contra-indicated in any case of anuria and it is too late to wait for evidence of nitrogen retention. The occurrence of a uretero-vaginal fistula may be immediate or delayed for weeks. In the authors' series the average time was the fourth post-operative day. Ureteral catheterization should be carried out without delay and either retrograde or intravenous pyelography will clarify the state of affairs.

The treatment depends upon the time of discovery and the type of damage. If the injury is found at the time of operation ligature of the ureter is best if the patient is unable to stand a further prolongation of the operation; otherwise an end-to-end anastomosis over a large indwelling catheter is the method of choice and the stream of urine may be diverted to the flank from a stab wound in the ureter above the site of injury.

In post-operative cases the authors recommend bilateral nephrostomy in bilateral occlusion as soon as possible. In unilateral cases there is no great haste and they advise that every effort is made to introduce a ureteral catheter past the site of injury. If the catheter cannot be passed to the kidney and there is evidence of good renal function, extraperitoneal re-implantation of the ureter into the bladder should be attempted; otherwise the kidney will have to be drained or, if infected, removed.

THE AETIOLOGY AND TREATMENT OF ENDOCERVICITIS AND CERVICAL EROSIONS.

In this paper Wollner gives a short description of the accepted textbook version of the train of events which leads up to the formation of an erosion. He then brings forward his theory that the cervical mucosa undergoes menstrual cyclical changes and that these changes are correlated with ovarian hormonal activity. To demonstrate this theory he describes his experimental studies on 6 women, whose cervical mucosa was subjected to the atrophic changes incidental to castration or the physiological menopause. He divided these 6 women into 3 pairs; those in group 1 were given oestrin daily, those in group 2 progestin only, and those in group 3 were treated with oestrin and progestin. Sections of the cervix were taken before treatment in every case and in all of them the usual atrophic changes were present.

The author observed that after surgical castration these changes occurred more rapidly than when the physiological menopause had taken place. Another cervical specimen was taken after the completion of the hormonal treatment. He reports his findings in these 6 cases in detail. Oestrin tended to stimulate the proliferation of the columnar cell elements, with hyperaemic and oedematous changes in the stroma. Large doses changed the atrophic mucosa into a picture of glandular hyperplasia, as seen typically in cases of endocervicitis. Progestin seemed to stimulate the growth of the squamous epithelial elements and this epithelium showed a pronounced tendency to invade the endocervical surface. The combination of oestrin and progestin altered the action of each individual hormone. Progestin seemed to exert a certain inhibitory effect on the action of oestrin, while oestrin

seemed to accentuate the progestin's stimulating effect on the squamous epithelium.

After discussing these findings, the author states that he believes that a great number of cases of so-called endocervicitis and erosion are merely cases of physiological changes in the cervical epithelia. He states that according to his observations, ovarian hormone action is capable of producing histological changes which have formerly been interpreted as inflammatory conditions. So-called endocervicitis and erosions are known to persist for many years without any tendency towards spontaneous cure and are resistant to the usual treatment of inflammatory conditions. He believes that this hormone conception will open a new approach to the treatment of cervical lesions.

HORMONE FACTORS IN THE TOXAEMIAS OF PREGNANCY.

Taylor and Scadron believe that the placental hormones are an important factor in the cause of late pregnancy toxaemias. Although these substances are present in the blood of non-pregnant women, their concentration is greatly increased during pregnancy. They feel that they are undoubtedly responsible for much that is specific in the physiology of the pregnant woman, especially in pre-eclamptic toxaemia and eclampsia. They discuss the hypothesis as to how the many manifestations of toxaemia may be brought about by the agency of these hormones. It may be due to a direct action of the placental hormones; to an intermediate effect through their influence on general metabolic processes; or as an intermediate effect through their influence on other endocrine glands, the posterior pituitary, the anterior pituitary, the adrenal, or the thyroid. The toxaemic symptoms may occur with normal concentrations of hormones, but the individual is especially susceptible to this concentration; these hormones may be qualitatively changed in the toxaemic patient; or the quantity of these hormones may be at fault, as high levels of prolan and low levels of oestrin have been reported in eclampsia.

In this paper the authors have studied the oestrogen and prolan in the blood and urine of 48 patients in the last few weeks of pregnancy in order to test these observations. They estimated the average values of serum and urine prolan in 17 normal patients around the thirty-seventh week of pregnancy and then they found that the majority of toxaemic patients had a rise in prolan, but that these findings were by no means uniform. As these findings did not agree with previous workers, the authors came to the conclusion that they were including some cases of chronic nephritis in their series. They picked out their more severe and definite cases of pre-eclampsia and eclampsia and they came to the conclusion that the prolan in the urine or serum was a little high. Similarly, the oestrogen values were estimated in normal and in toxaemic patients and they came to the conclusion that, in the later group, there was a significant lowering of these values. However, there was nothing in these estimations to distinguish the severe cases from the mild ones. As abnormal values of corpus luteum hormones in the

placentae of toxaemic patients had been reported by others, the authors estimated the amount of excretion of pregnandiol in normal and in toxaemic patients. They found that there was a definite lowering of this excretion in the latter group. In 8 cases of unexplained antepartum bleeding and in 2 cases of premature separation of the placenta they found no hormone abnormality.

In the discussion of their findings, the authors agree that probably there is an increase of prolan and a decrease of oestrin in the blood or in the urine in cases of toxaemia. However, they feel that this disturbed balance between these hormones may be the result of the disordered physiology of the toxaemic patient and not the cause of the toxaemia.

Bryan Jeaffreson.

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Vol. cxiii, No. 18, October 28th, 1939.

The treatment of retrodisplacements of the uterus. W. T. Dannreuther.
Cardiac asthma and acute pulmonary oedema complicating toxaemias of pregnancy. Duncan E. Reid and Harold M. Teel.

Vol. cxiii, No. 23, December 2nd, 1939.

Obstetric analgesia. Jacob Kotz and Morton S. Kaufman.
*Neonatal asphyxia. W. C. C. Cole, David C. Kimball, and L. E. Daniels.
Dermatitis following theelin. Louis A. Levison and Julius J. Harrison.

Vol. cxiii, No. 26, December 23rd, 1939.

*A clinical study of stilboestrol. Ephraim Shorr, F. H. Robinson, and G. N. Papanicolaou.
Effects of diethylstilboestrol therapy. C. L. Buxton and Earl T. Engle.
Studies on stilboestrol. Cyril M. MacBryde, Harold Freedman, and Ellen Loeffel.

Vol. cxiii, No. 27, December 30th, 1939.

Hyperparathyroidism and pregnancy. Clifford L. Spingarn and S. H. Geist.

Vol. cxiv, No. 1, January 6th, 1940.

Necrosis of the anterior pituitary following parturition. H. C. Gotshalk and I. L. Tilden.

NEONATAL ASPHYXIA.

After analysing 5,000 consecutive hospital deliveries, the authors conclude that the most important single factor in the production of neonatal asphyxia is prematurity. This is followed in importance by trauma, while sedatives and anaesthetics increase the tendency to asphyxia in direct proportion to the amounts given.

A CLINICAL STUDY OF STILBOESTROL.

Clinical trial shows that this compound is an active oestrogen capable of inducing follicular smears, vaginal cornification and withdrawal bleeding in amenorrhoea and the menopause, and it is also capable of relieving the subjective symptoms of the menopause. Less active than oestradiol benzoate parenterally, stilboestrol is more active than the natural oestrogens by mouth, losing only about one half of its activity when given by this route. It is, however, less active than ethinyl oestradiol by oral administration.

The present investigation showed that toxic effects occurred in no less than 80 per cent of the patients treated, a considerably greater proportion than is mentioned by English writers on this subject. The toxic effects were central in origin, and followed either oral or parenteral administration of stilboestrol. They consisted of nausea, vomiting, abdominal distress, anorexia, diarrhoea, lassitude, paraesthesiae, vertigo, thirst, psychotic reactions and cutaneous rashes. There was no evidence that a tolerance to the drug could be achieved, and the severity of the toxic symptoms was unrelated to the size of the dose.

The authors conclude that until these toxic side effects have been more thoroughly investigated, the use of the drug in humans should be confined to experimental studies by qualified investigators.

F. H. Finlaison.

Surgery, Gynecology and Obstetrics.

Vol. lxx, February, 1940, No. 2A.

The management of chronic pelvic infections. George H. Gardner, M.D., F.A.C.S., Chicago, Illinois.

*Prophylaxis and treatment of carcinoma of the cervix and body of the uterus. Willard R. Cooke, M.D., F.A.C.S., Galveston, Texas.

Endocrine therapy in obstetrics and gynaecology. John C. Burch, M.D., F.A.C.S., Nashville, Tennessee.

*The management of pelvic dystocia. Alfred C. Beck, M.D., F.A.C.S., Brooklyn, New York.

*Toxaemias of pregnancy. Herman W. Johnson, M.D., F.A.C.S., Houston, Texas.

Vol. lxx, March, 1940, No. 3.

Foetal swallowing, gastro-intestinal activity and defaecation *in amnio*; an experimental Roentgenological study in the guinea-pig. R. F. Becker, M.S., W. F. Windle, M.S., Ph.D., E. E. Barth, M.D., and M. D. Schultz, M.D., Chicago, Illinois.

*Management of breech delivery. Thomas R. Goethals, M.D., Boston, Massachusetts.

*A consideration of so-called *granulosa* and *theca* cell tumours of the ovary. Herbert F. Trait, M.D., and Andrew A. Marchetti, M.D., New York.

The anatomy of the subperitoneal tissues and ligamentous structures in

relation to surgery of the female pelvic viscera. Arthur H. Curtis, M.D., F.A.C.S., Barry J. Anson, Ph.D. (Med. Sc.), and Linsay E. Beaton, M.D., Chicago, Illinois.

*Anaesthesia in Caesarean section. Kenneth M. Heard, M.B., D.A., F.I.C.A., Toronto, Canada.

*Infected ectopic pregnancy, infected pelvic haematocele. H. C. Falk, M.D., F.A.C.S., and George Blinick, M.D., New York.

Vol. lxx, April, 1940, No. 4.

*Concepts of a new classification of ovarian tumours. Walter Schiller, M.D., Chicago, Illinois.

*The treatment of spontaneous, threatened, or habitual abortion. Conrad G. Collins, B.S., New Orleans, Louisiana.

*The effect of nitrous oxide, oxygen and ether anaesthesia upon the oxygenation of maternal and foetal blood at delivery. Clement A. Smith, M.D., Brookline, Massachusetts.

*Non-surgical closure of vesico-vaginal fistula. Vincent J. O'Conor, M.D., F.A.C.S., Chicago.

Endometriosis (Editorial). Virgil S. Counseller, M.D., F.A.C.S., Rochester, Minnesota.

PROPHYLAXIS AND TREATMENT OF CARCINOMA OF THE CERVIX AND BODY OF THE UTERUS.

While there has been a definite reduction in the incidence and mortality of cancer of the uterus, especially of the cervix, managed throughout by thoroughly competent gynaecologists, the general mortality rate from these conditions shows little or no improvement. At present this is due to the failure of the profession at large to recognize and treat the conditions predisposing to cancer of the visible areas of the cervix, and to resort to biopsy in all doubtful cases. The greatest hope for reduction of the rates of incidence and mortality of cancer of the uterus lies in routine examination every 6 months and promptly upon the appearance of any abnormal bleeding or discharge between these periodic examinations of all women over 30 years of age, in the recognition and treatment of heteroplasia and leucoplasia, and in the employment of biopsy in all cases of doubtful diagnosis.

In the treatment of actual cancer of the cervix, combined radium and Roentgenotherapy is the method of choice. Adequate Roentgenotherapy requires (1) complete co-operation between the gynaecologist and radiologist, (2) special high-voltage equipment and (3) a technique employing the principle of proper exposures through multiple portals.

Complete hysterosalpingo-oöphorectomy remains the generally accepted method of choice in the treatment of carcinoma of the endometrium. Since this condition does not require the very difficult and dangerous extirpation of the pelvic lymphatic areas, the mortality rate is low. It is possible that in the future the development of new principles in the application of radiation to this condition may result in its adoption as the method of choice.

THE MANAGEMENT OF PELVIC DYSTOCIA.

The possibility of pelvic dystocia should be recognized by measurement of the pelvis during the prenatal period. External measurements are of little value in determining whether a pelvis is or is not contracted. The diagnosis depends upon the length of the diagonal conjugate and the bi-ischial diameters, or upon the measurements obtained by one of the accurate Roentgenographic techniques.

It is hoped that every woman will have the size of her pelvis determined by means of Roentgenography before she is married or when she becomes pregnant just as she is having a premarital or prenatal Wassermann test done at the present time.

Elective Caesarean section is advised when the true conjugate diameter is 8 centimetres or under. Borderline cases of pelvic contraction are given a trial labour and the decision either for or against Caesarean section must be made within 15 hours after the onset of labour and within 4 hours after the membranes have ruptured. The use of stereoscopic Roentgenographic studies in the course of the trial labour is advised. A full test of labour is not necessary in the majority of borderline pelvic contractions.

The low Caesarean section is not safe when it is done too late in labour, long after the membranes have been ruptured, and after vaginal manipulations have been made. It is a relatively safe procedure when it is done within 10 to 15 hours after the onset of labour and within 4 hours after the membranes have ruptured, provided no vaginal examinations have been made and a good technique has been followed throughout the trial labour period. A destructive operation sometimes requires more skill than is required for the performance of the Caesarean section. A destructive operation cannot always be done in a neglected case of pelvic dystocia without risk to the mother. Even in neglected cases, Caesarean section often can be performed successfully, but the risk to the mother is too great to warrant its use in such circumstances if she can be delivered by any less dangerous procedure.

High forceps, podalic version, and the induction of labour are not recommended in the management of contracted pelves.

TOXAEMIAS OF PREGNANCY.

The suggestion is made that the specialty of allergy may be instrumental in solving the aetiology of hyperemesis gravidarum. The theory regarding eclamptic toxaemia which the authors have tried to support requires that (1) stasis in the intervillous spaces must be of sufficient duration to cause degeneration of chorionic tissue, with the production of tyrosine; (2) that only through infective processes with bacteria or enzymes circulating in the blood is the conversion of tyrosine to tyramine possible; (3) the absorption of the tyramine formed depends on the condition of uniform pressure as outlined in the paper; (4) tyramine circulating in the blood in pregnancy produces only hypertension; and (5) in the sensitive or allergic patient, tyramine produces hypertension, plus capillary spasm which is the pathological unit of eclampsia.

Management of Breech Delivery.

The management of breech presentation has been discussed based upon the corrected statistics obtained from a study of 2,035 pelvic breech deliveries and 58 abdominal Caesarean sections in the Boston Lying-in Hospital from 1888 to 1937 inclusive.

The author concludes that about 7 per cent of primigravidae with breech presentations at term should be delivered by Caesarean section. Roentgenographic mensuration of the foetal head *in utero* has a definite, if limited, value in helping to diagnose foeto-pelvic disproportion. The ideal method of making a comparison of the foeto-pelvic relation in breech presentation has not yet been determined.

The statistics and experience derived in this study indicates that, if delivery through the pelvis is selected as the method of choice, the second stage of labour should be terminated by breech extraction under full surgical anaesthesia before the birth of the umbilicus, as has been classically recommended, has occurred.

Granulosa and Theca Cell Tumours of Ovary.

A study of 54 ovarian tumours of the theca granulosa cell group is reported. The use of Foot's silver stain makes possible the differentiation of theca from granulosa cells in most instances. So-called granulosa cell tumours contain varying amounts of theca cell elements as well, so that pure granulosa cell tumours are rare. Most tumours contain from a quarter to a third of their differentiated cells in the form of theca cells. A number of tumours was encountered which had equal representations of the two cell types, while most so-called theca cell tumours also contained granulosa elements in considerable representation. One pure granulosa cell tumour and four pure theca cell tumours are described. An attempt is made to outline the life cycle of these tumours and its relation to the clinical syndrome they present.

Anaesthesia in Caesarean Section.

In the mother, pulmonary and cardiac complications are not markedly influenced by the type of anaesthetic. This is in accordance with the now universally recognized fact that pulmonary complications vary primarily with the site of operation and length of time on the table. Consequently the tendency will be for the surgeon or anaesthetist to use the anaesthetic which he prefers for ordinary abdominal work, such as hysterectomy. The man who dislikes spinal anaesthesia in one will probably avoid it in the other. Perhaps this is not unreasonable, since there is an old dictum that the safest anaesthetic is the one with which the individual is himself adept. However, this must not be carelessly carried to the point of endangering the baby, whose safety demands the avoidance of ether. The bad effect of ether reaches its peak in the abnormal baby or with heavy sedation in the mother. Ether can be avoided simply and easily by the use of spinal anaesthetics or,

with much greater difficulty, by the use of gas alone. General anaesthesia is best avoided unless the obstetrician is reasonably sure that the baby is normal and the anaesthetist confident that he can complete the work with gas alone. He who denies the baby the safety of spinal anaesthesia must accept the responsibility of protecting him from ether; for if this article is not to be interpreted as an argument for spinal anaesthesia, it is at least a condemnation of ether.

Infected Ectopic Pregnancy.

The most common source of suppuration complicating haematocoele is infection subsequent to intra-uterine manipulation. Infection may also spread from the rectum and intestines or from a co-existing salpingitis.

Pelvic haematocoele which causes sufficient symptoms to require operation is most commonly caused by ectopic pregnancy. However, only 50 per cent of the patients presented had histological proof of extra-uterine gestation. The most constant symptom is persistent and irregular vaginal bleeding. Pain, fever, history of a missed period, and a pelvic mass may be present. The laboratory findings are essentially those of infection and haemorrhage. The signs and symptoms resemble those of any type of pelvic infection and the condition is often misdiagnosed as parametritis, pyosalpinx, infected ovarian cyst, etc. The blood usually becomes encysted before infection takes place. Subsequently, there is a fusion of the wall of the mass with the adjacent layer of visceral or parietal peritoneum, a circumstance which has given rise to the mistaken belief that infected haematocoele is primarily extraperitoneal in nature. When feasible, posterior colpotomy is the treatment of choice. When the infected mass must be operated on transabdominally, simple incision and drainage at the site of adherence to the parietal peritoneum is safer and preferable to complete excision, except in selected cases. Infection of pelvic haematocoele causes a marked increase in the mortality rate of ectopic gestation. Many cases are not recognized and death is ascribed to pelvic abscess, sepsis, or peritonitis. In this series of 10 cases there were 2 deaths, a gross mortality of 20 per cent.

New Classification of Ovarian Tumours.

Schiller's suggested classification of ovarian tumours is self-explanatory.

Cysts. (*a*) Follicular; (*b*) Corpus luteum; (*c*) Corpus atreticum, luteinized —lutein cysts.

True Tumours.

(*A*) Ovariogenic—derived from ovarian tissue. (*a*) Granulosa cell tumour: (1) Homogeneous; (2) trabeculated; (3) follicular. (*b*) Fibroma: (1) Simple; (2) luteinized—xanthofibroma thecacellulare. (*c*) Myoma, angioma, luteinoma.

(*B*) Heterotopic—derived from tissue not normally present in ovary. (*a*) By pathological differentiation. (1) From surface epithelium—prosoplasia in direction of muellerian duct: (i) Serous cystoma—Fallopian tube; (ii) endo-

metrioma—endometrium; (iii) pseudomucinous cystoma—cervix. (2) From mesenchymal core by error in sex chromosomes: (i) Arrhenoblastoma—male; (ii) dysgerminoma—neutral. (*b*) From displaced uterus. (1) In foetal life: (i) Early—teratoma; mature, e.g. dermoid; immature—embryoma; (ii) Late —tissue from vicinity: Ganglioneuroma, hypernephroma, mesonephroma, Brenner's tumour—urogenital epithelium. (2) In adult life: (i) By implantation—endometrioma; (ii) by metastases of malignant tumours—e.g. Krukenberg carcinoma.

The cystomata of *B, a,* 1, i–iii are to be characterized as unilocular or multilocular, and as simple or papillomatous.

The surface papilloma may be classified under *B, a,* 1, i, papillomatous, the folliculoma lipidique Lecene tentatively under *A, a,* the myxoma under *B, b,* 1.

The arrhenoblastoma of *B, a,* 1, i, may be characterized as homogeneous, trabeculated or adenomatous-testicular.

Treatment of Abortion.

The authors submit that wheat-germ oil therapy forms a valuable basis for the treatment of spontaneous and/or habitual abortion. It should be fortified by the administration of progestin and/or thyroid extract when necessary.

The fear of delivering a malformed foetus in cases in which spontaneous or habitual abortion has been successfully combated is over-emphasized.

All efforts should be made to control spontaneous abortion or habitual abortion by the use of all known remedies which have been proved of value. They present their results in 36 patients so treated to substantiate our views.

Effect of Nitrous Oxide-Oxygen-Ether at Delivery.

In 28 infants delivered under nitrous oxide, oxygen and ether anaesthesia, the oxygen content of umbilical cord blood at the moment of birth was determined. Measurements were made upon samples from the umbilical vein (foetal arterial blood) in all infants and upon samples from the umbilical arteries (foetal venous blood) in all but 2. Simultaneous specimens were obtained from the maternal arm veins in 10 and from the maternal radial artery in 6 instances. Apparently the analyses were sufficiently accurate to be significant, although the presence of ether may have resulted in values slightly above the actual oxygen level present, particularly in the maternal specimens.

As compared with results from deliveries under ether anaesthesia alone, these mothers and infants showed a significantly diminished degree of oxygenation. The results were almost identical with those from a series of deliveries under nitrous oxide and oxygen alone.

The infants born under nitrous oxide, oxygen and ether had as much nitrous oxide in their blood as did those born under nitrous oxide and

oxygen alone, though this gas was present at a lower level in the maternal blood of the former group than of the latter.

Usually, although not always, foetal anoxaemia was associated with apnoea at birth. Occasionally infants born with such low oxygen levels as 2.6 volumes per cent in the arterial blood, breathed and cried actively at once. In such instances the anoxaemia must be only of brief duration.

Judging by the amount of oxygen reaching the foetus at birth, the data presented indicate oxide and oxygen alone or combined with ether to be a less satisfactory obstetrical anaesthesia than ether alone.

NON-SURGICAL CLOSURE OF VESICO-VAGINAL FISTULA.

The authors conclude that small vesico-vaginal fistulae with healthy surrounding tissue will heal after electro-coagulation, if postural drainage can be maintained with an indwelling catheter for a sufficient period of time. The possibility of this method should receive more consideration, especially in patients upon whom an unsuccessful surgical repair has resulted in a small lateral opening. The method obviously has no place in the treatment of fistulae of the vesical floor or in patients with extensive tissue defects.

Charles D. Read.

Gynécologie et Obstétrique.

Vol. xl, No. 4, 1939-40.

*True prolongation of pregnancy. A. Fruhinsholz and J. Richon.
Labour in sportswomen. J. L. Audebert.
*Endometriosis and pregnancy. L. Portes and J. Varangot.
An anatomical-clinical classification of cervicitis. P. Durel, V. Ratner, and A. Deroin.
*The iron metabolism of the foetus. W. Neuweiler.
*Vitamin C exchanges in pregnancy and the puerperium. J. F. De Rezende.
Neurofibromatosis and pregnancy. B. Triantafillopoulo.
Henry's reaction for Paludism in pregnancy. Marie Reniger-Areschian.

TRUE PROLONGATION OF PREGNANCY.

Fruhinsholz and Richon refer to a previous paper (*Gynécologie et Obstétrique*, July 1939), in which they laid down certain conditions which must be observed before pregnancy may be assumed to be unduly prolonged. These conditions are a reliable patient, a regular menstrual cycle and delivery occurring at least 300 days after the beginning of the last period.

True prolongation of pregnancy appears to be more common than was supposed. Since 1930 the authors have seen 128 cases out of 1,200 deliveries. The longest period they observed was 351 days. Only 47 mothers gave a

perfectly normal family and individual history. In 14 cases one or other of the parents had died between 30 and 55 years from sudden death or mental disease, and in the fraternities to which the mothers belonged there was a foetal and neonatal mortality of 28 per cent.

The following maternal somatic stigmata were noted: obesity, four cases; dwarf, one case; degenerate, one case; thyrotoxicosis, one case; epilepsy, one case; squint, three cases; congenital dislocation of the hip, one case; congenital deformity of the hand, one case; hirsutes, one case; congenital ptosis, one case.

Four of the children weighed 2,000 to 2,500 gms., 24 2,500 to 3,000 gms., 37 3,000 to 3,500 gms., 40 3,500 to 4,000 gms., and 5 4,500 to 6,000 gms.

The majority of the foetûs were normal. There was one intestinal malformation. In contradistinction to previous writers the authors did not find a high incidence of foetal malformations. The foetal mortality was about 10 per cent as compared to an average of 7 per cent; 7 out of the 13 stillbirths were macerated, and the raised foetal mortality appears to be largely independent of difficulties in delivery. It would appear that these infants are more fragile than normal.

The paper is particularly interesting in two regards, the absence of foetal malformations in the series and the fact that severe dystocia was not encountered in any case.

Endometriosis and Pregnancy.

Portes and Varangot describe one case of endometriosis and pregnancy and review the literature of the subject. They conclude that although it is rare to find any endometrial tumour associated with a pregnancy, histological examination shows that a decidual endometrial reaction of the ovaries and pelvic peritoneum is quite common. In their own case the authors performed Caesarean section followed by hysterectomy. The combination of the two conditions of pregnancy and endometriosis is almost invariably found in elderly primigravidae.

Iron Exchange of the Foetus.

Neuweiler describes the method of spectroscopic analysis of the iron content of the serum of mother and foetus. He found that the maternal values for the serum-iron were between 50 and 151 per cent with an average value of 93 per cent.

He confirmed the high iron value of the cord-serum, observed by former workers, the range being 84–240 per cent. He could not establish any correlation between the foetal serum-iron, the haemoglobin and the number of red corpuscles. A higher value was obtained for the venous blood in the cord as compared with the arterial blood in the cord. In some cases in which a low value was obtained for the maternal blood, the value was relatively high in the foetus. He concludes that the results show that the foetal iron is not derived directly from the maternal haemoglobin.

VITAMIN C IN PREGNANCY AND THE PUERPERIUM.

De Rezende, of Rio de Janeiro, contributes a paper based on a paper by Rotter. (Rotter, H., *Nature*, 139, 717, 1937.)

This test depends upon the intradermal decoloration of a dyestuff, 2:6 dichlorophenol-indophenol, the decoloration of which appears to vary with the amount of ascorbic acid present. In patients saturated with ascorbic acid decoloration occurs within five minutes, and in patients with a deficiency 10 minutes at least is needed. An intradermal injection of 1/60 c.c. of an 80 per cent solution of dichlorophenol-indophenol is given in the skin of the forearm. The test shows a relative deficiency in pregnancy and the puerperium of vitamin C, a deficiency becoming more pronounced towards the end of pregnancy. In the puerperium the deficiency is more marked in sick women, and particularly in women with white legs.

The author leaves the question undecided whether the deficiency in vitamin C exhibited by pregnant women represents the real pathological state or whether it is to be interpreted merely as a normal modification of the physiological balance. A bibliography is appended.

Percy Malpas.